HEALTH POLICY AND MEDICAL RESEARCH: HEPATITIS B IN THE UK SINCE THE 1940s

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ABSTRACT

Health policy and medical research: hepatitis B in the UK since the 1940s

This thesis explores the way changing constructions of hepatitis B have mediated between science and policy during the past fifty years. Research-based 'facts' were filtered in the policy arena according to social, political and economic pressures. Central policy processes depended heavily on expert advisers, who emerged from networks of researchers. This account draws on scientific, clinical and epidemiological research, central policy documents, and interviews with people working with or suffering from the disease.

Though epidemiologically close to AIDS, hepatitis B has rarely attracted public attention: there are an estimated 100,000 carriers in the UK, but few deaths due to the acute form. The disease was a major problem in the blood supply, and featured as a hospital infection, with notable outbreaks from 1965 in renal dialysis units. It was seen as an occupational hazard for laboratory workers, doctors, nurses and dentists.

The introduction of a test for hepatitis B around 1970 opened up opportunities for epidemiological research. Hepatitis B was increasingly recognized as a sexually transmitted disease, widespread among gay men; also, because of needle sharing, prevalent among drug users. Another outcome of research in the 1970s was the development of a vaccine.

However, availability of a vaccine in the UK from 1982 afforded no immediate resolution of public health issues raised by hepatitis B. The legacy of a restricted screening policy from the 1970s, emphasizing prevention via hygiene precautions among health care workers, facilitated a limited vaccine policy throughout the 1980s.

While discussing negotiations over hepatitis B in the past five decades, this thesis aims to contribute to a broader analysis of interactions between science and policy, between centre and regions, and between interest groups.

CONTENTS

PREFACE

The preparation of this thesis would not have been possible without a wide range of support. The research originally arose from a proposal put forward to the Wellcome Trust by Dr Phil Strong and Dr Virginia Berridge, entitled 'The history of hepatitis B policy in the United Kingdom 1960s - 1980s'. The Trust provided funding for three years (Grant no: 031287), for my post as a Research Fellow attached to the AIDS Social History Programme, in the Health Policy Unit at the London School of Hygiene and Tropical Medicine (LSHTM). During this time, Oct 1990 - Sept 1993, I was a Research Associate at the Wellcome Unit for the History of Medicine, Oxford: I am most grateful for their provision of office accommodation. The Health Policy Unit at LSHTM kindly underwrote my salary for three months, Oct - Dec 1993.

These institutional attachments offered rich and varied intellectual environments, further enhanced by opportunities to give papers as my research progressed in a variety of outside groups, notably the Wellcome Twentieth Century History of Medicine Group, the Science Museum, and a conference at Annecy organised by l'Institut Louis Jeantet de l'Histoire de Medicine.

Among the many individuals who have given me information and advice, or practical help - all of whom I thank - I would like to mention in particular: Profesor Baruch Blumberg, for patiently explaining the basics when I began, and agreeing to further interviews later; Dr David Dane, for a sustained correspondence answering awkward questions that occurred to me as I wrote; Dr John Barbara, for his explanation of the mathematics of testing; Miss Deborah Torrance, archivist at the Medical Research Council, for exhuming files that were about to be transferred to the Public Records Office; and Ms Janet Foster, archivist to the AIDS Social History Programme, for passing on leads of relevance to hepatitis B. I am grateful to Dr Dorothy Porter and Dr Martin McKee for sitting on the upgrading committee in May 1992. Above all I wish to thank my colleague and supervisor Dr Virginia Berridge, for consistent encouragement, feedback and academic support.

None of these thanks indicates that anyone other than myself is responsible for what is written here, including errors; or for any omissions.

Note: Before 1992, I was known and published under the name 'Beinart' and thereafter under the name 'Stanton'.

ABBREVIATIONS

AGH	Advisory Group on Hepatitis
AIDS	Acquired immunodeficiency syndrome
ASTMS	Association of Scientific, Technical and Managerial Staffs
BMA	British Medical Association
BPL	Blood Products Laboratory (after 1990: Bio Products Laboratory)
BTC	Blood Transfusion Centre
CDSC	Communicable Disease Surveillance Centre
DHSS	Department of Health and Social Security
DoH	Department of Health
EM	Electron microscopy
FPC	Family Practitioner Committee
GP	General practitioner
HBsAg	Hepatitis B surface antigen
HBIG	Hepatitis B immunoglobulin
HIV	Human immunodeficiency virus
HMSO	His/Her Majesty's Stationery Office
IVDUs	Intravenous drug users
LSHTM	London School of Hygiene and Tropical Medicine
MHIs	Mental handicap institutions
MRC	Medical Research Council
NHS	National Health Service
NIH	National Institutes of Health (US)
NLBTC	North London Blood Transfusion Centre
PHLS	Public Health Laboratory Service
RCN	Royal College of Nursing
SSK	Sociology of scientific knowledge
WHO	World Health Organisation

CHAPTER 1: INTRODUCTION

The aim of this thesis is to contribute to the historical understanding of health policy formation in relation to advances in scientific medicine. This has remained an insufficiently explored area, although many historians of medicine have embraced the research-policy axis in some form.[1] Especially for the postwar period, Berridge has identified a 'need to establish work relating medicine to its policy context'.[2] Writing of social, rather than biomedical, science in relation to policy, Berridge and Thom set an agenda:

> This is the central problem, to understand the process by which knowledge is generated and used by different groups and the social, political and economic forces which help to shape the selection and interpretation of information at different periods of time.[3]

The present study aims to make a modest contribution to this large and ambitious programme, by focussing on the postwar history of research and policy around hepatitis B. The periodisation is determined less by a tendency to see the Second World War as a 'watershed' for medicine, a tendency persuasively countered by Lawrence,[4] than by the history of

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[1] See, for example: C. Webster (ed.), Biology, medicine and society 1840-1940 (Cambridge: Cambridge University Press, 1981) and literature on medical innovations outlined below.

[2] V. Berridge, 'Health and medicine in the twentieth century: contemporary history and health policy', Social History of Medicine 5,2 (August 1992), pp. 307-16; p. 311.

[3] V. Berridge and B. Thom, 'The relationship between research and policy: case studies from the post war history of drugs and alcohol', paper for International Congress on Social History of Alcohol, London Ontario, May 1993, to be published in Contemporary Drug Problems (forthcoming); typescript, p. 7.

[4] C. Lawrence, Medicine in the making of modern Britain, 1700-1920 (London and New York: Routledge, 1994), p. 2; but see opening section of Chapter 3, below.

recognition of the disease itself.

Why study the history of one particular disease? Such a project might appear constricting to those familiar with histories of medical professions, of developments in technique and technologies, medical institutions, and health services; set in the framework of twentieth century changes in provision of health care, influenced by two world wars, recession, changing relations of production and colonial power.[5] Why, with all this wealth of material, limit oneself to the study of one disease: would that not be terribly narrow? Of course there has been work on epidemic diseases with obvious social impact like cholera.[6] Work on other, more endemic diseases has spoken on social policy, on public attitudes, on power and prejudice in organization of treatment - for example tuberculosis and venereal diseases have provided rich minefields for social historians.[7] But these are illnesses with broad social ramifications. What can be made of a

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[5] Other subject areas could be mentioned; those selected here reflect the author's own previous work, listed under 'Beinart' in the Bibliography.

[6] R. J. Morris, Cholera 1832: The social response to an epidemic (London: Croom Helm, 1976); M. Pelling, Cholera, fever and English medicine 1825-1865 (Oxford: Oxford University Press, 1978); M. Durey, The return of the plague: British society and the cholera 1831-2 (Dublin: Gill and Macmillan, 1979). See also: T. O. Ranger and P. Slack (eds), Epidemics and ideas (Cambridge: Cambridge University Press, 1992); C. E. Rosenberg, Explaining epidemics and other studies in the history of medicine (Cambridge: Cambridge University Press, 1992)

[7] See for example: L. Bryder, Below the magic mountain: a social history of tuberculosis in twentieth-century Britain (Oxford: Clarendon Press, 1988); A. M. Brandt, No magic bullet: a social history of venereal disease in the United States since 1880 With a new chapter on AIDS (New York: Oxford University Press, 1987)

disease which lacks its own distinct identity, distinguished from other diseases sharing the same name only by a letter of the alphabet?

Nomenclature apart, hepatitis B in fact does have a very distinctive identity; moreover, any disease, from the common cold to AIDS, may be studied in as narrow or broad a context as one may choose. Two things have to be said at this point. First, the nature of the disease shapes the agenda to some extent: we are talking here of an infectious disease - like syphilis, say - not an hereditary disease like diabetes or a disease like cervical cancer, with complex etiology perhaps involving environmental factors. There are public health implications common to infectious diseases: for example, when the route of infection is traced, prevention by separating carriers from others or by behaviour change may be on the agenda; and when an agent is identified, there may be hope of developing a cure (in the case of bacterial agents), or a vaccine, with further preventive possibilities. In this case, we are dealing with a viral disease with no cure, but with a vaccine becoming available in the 1980s.

Second, hepatitis B is very close, epidemiologically, to HIV. This has many ramifications, but most immediately important for shaping the present study is its origin in a proposal from the AIDS Social History Programme, which provided a model of a broad, social history approach with an emphasis on policy

issues.[8] The closeness of hepatitis B to HIV suggests that there will be an audience looking for lessons from the history of hepatitis B to enlighten the AIDS story, and perhaps to inform current AIDS policy, but that is not the chief purpose of the present study. Historians working in a wide variety of fields other than AIDS may find something relevant here - for hepatitis B, like AIDS, touches on an enormous range of issues and activities, too many to cover thoroughly in a single account. General issues with resonances for AIDS history cluster around the general theme of the thesis, that is, the way that the nature of the disease is socially constructed, with the apparently firm facts emerging from research selectively adapted to policy formation by various interest groups.

Specific issues appear at certain points. These were not always those written into the original plan, but arose from the material: the ethics of human experimentation (Ch.2); how researchers link informally and provide expert input into policy making (Chs 3 and 6);[9] the crucial role of a nationwide public health laboratory service (Ch.4); whether government reluctance to spend on the UK blood products laboratory cost lives (Ch.5); Britain's underestimated research contribution (Chs 3 and 6); individual rights of health workers to

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[8] See Preface; for outcome of the AIDS project in terms of history, see: V. Berridge, The history of the present (Oxford: Oxfrod University Press, forthcoming), plus interim papers.

[9] See also: J. Stanton, 'Blood brotherhood: techniques, expertise and sharing in hepatitis B research in the 1970s', in G. Lawrence (ed.), Technologies of modern medicine (London: Science Museum, 1994), pp. 120-33.

confidentiality, and to avoid testing, versus the public health interest (Chs 7 and 8); how vaccine policy is formulated (Ch.8);[10] the role of expert groups (Chs 2, 8 and passim).[11] Together these discussions shed light, if obliquely, on funding and organization in the health services, especially the infrastructure of diagnostic laboratories and the blood supply; also on relations between publicly funded medical research, in academic or clinical laboratories, and privately funded research in pharmaceutical laboratories. More research is needed, however, on these issues. The conclusions reached here on ways that health policy interrelates with medical research will be in the nature of hypotheses requiring further testing.

Literature review

(a) Scientific medicine

(i) General contextualization

Science is not set apart from other sorts of productive activity but its special character is explored in the growing field of sociology of scientific knowledge (SSK). Recently, awareness has grown of the complexity and messiness of

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[10] And: J. Stanton, 'What makes vaccine policy? The case of hepatitis B in the UK', Social History of Medicine, 7,3 (December 1994), 427-46.

[11] Most clearly formulated in: J. Stanton, 'A jaundiced view: medical experts and hepatitis committees, 1943-1993', paper for 'Doctors and the state' seminar, Wellcome Institute for the History of Medicine, London, 21 Jan 1994.

scientific research, of the need to look at the daily activities taking place around the laboratory bench, or conversations at the drinking-water fountain as well as phone calls to journal editors - anthropological rather than biographical perspectives. For example, Latour and Woolgar examined the whole configuration of 'inscription devices' - equipment and materials laid out around the laboratory - which led to the definition of a new scientific 'fact'.[12] Studer and Chubin's study of cancer research concentrated on the way scientists used each others' written work, using a highly sophisticated technique of 'citation analysis'.[13] A broader analysis of networking is provided in Fujimara's study of how cancer researchers devise a feasible research project, taking into account not only what is technically possible but what will appeal to funding bodies.[14]

To some extent this blossoming of SSK is reflected in corresponding studies in history of science and medicine, although few historians have spent lengthy periods observing activities in laboratories: only the very recent past can be accessed that way. Rather, we have seen the development of

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[12] B. Latour and S. Woolgar, Laboratory life: the social construction of scientific facts (Beverly Hills and London: Sage Publications, 1979); see also B. Latour, Science in Action (Milton Keynes: Open University Press, 1987)

[13] K. E. Studer and D. E. Chubin, The cancer mission: the social context of biomedical research (Beverly Hills and London: Sage Publications, 1980)

[14] J. Fujimura, 'Constructing "do-able" problems on cancer research: articulating alignments', Social Studies in Science, 17 (1987), 257-93. See also: Mel Bartley, 'Do we need a strong programme in medical sociology?', Sociology of Health and Illness, 12 (1990), 371-90.

equally imaginative approaches to problems of historical understanding that were previously described in non-analytical, unilinear modes - particularly medical innovations and biomedical research.[15] Recent work, informed by SSK but with more emphasis on biography, has shown the value of considering the social and economic relations of medical scientists and doctors. As Lowy says: 'The historiographers of biomedical laboratories follow actors and practices, not "discoveries" or the "progress of science"', which may result in a more complicated, even confusing picture than the traditional 'temple of science' account.[16] Such a picture may, however, provide a more fitting counterpart to the world of political pressures involved in health policy making.

While there is a growing body of literature on specialization in medicine, showing how edifices of professional interests are built and defended,[17] there seems to be a lack of a parallel literature on professionalization of medical research - that is, the institutional rather than the productive aspects of medical research. Whole-institution or macro-studies, such as that of the state-funded Medical Research

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[15] J. V. Pickstone (ed.), Medical innovations in historical perspective (Basingstoke: Macmillan, 1992); I. Lowy (ed.), Medicine and change: historical and sociological studies of medical innovation (London: John Libbey, 1993)

[16] I. Lowy, 'Recent historiography of biomedical research', in G. Lawrence (ed.), Technologies of modern medicine (London, Science Museum, 1994), pp. 99-110, esp. p. 106.

[17] For example: G. V. Larkin, Occupational monopoly and modern medicine (London: Tavistock, 1983); or for a more sociological approach: M. Stacey, M. Reid, C. Heath and R. Dingwall (eds), Health and the division of labour (London: Croom Helm; New York: Prodist, 1977)

Council,[18] have so far failed to satisfy the need for contextualization; perhaps, as with studies of innovation, case studies will yield more fruitful results. Breadth or sharpness of focus are not in themselves defining criteria for useful work, however. Two influential monographs on relations between industry and medicine vary in this respect: Liebenau addresses a broad issue - the development of the pharmaceutical industry in America - while Blume selects certain diagnostic imaging technologies, but both provide context, analysis, and insights with useful comparative implications.[19]

The recently burgeoning 'pre-history of AIDS' has produced valuable insights on historical cases which illuminate hepatitis B as well as AIDS, such as Lowy's paper on changing views of the efficacy of the Wasserman test for syphilis.[20] Less historical but still relevant has been work on expensive medical technologies, for instance Stocking's comparative study of the application of lithotropy and other innovative techniques in several European countries.[21] Finally, of

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[18] J. Austoker and L. Bryder (eds), Historical perspectives on the role of the MRC (Oxford: Oxford University Press, 1989)

[19] J. Liebenau, Medical science and medical industry: the formation of the American pharmaceutical industry (Basingstoke: Macmillan, 1987); S. Blume, Insight and industry. On the dynamics of technological change in medicine (Cambridge, Mass: MIT Press, 1991; London, 1992)

[20] I. Lowy, 'Testing for a sexually transmissable disease, 1907-1970: the history of the Wasserman reaction', in V. Berridge and P. Strong (eds), AIDS and contemporary history (Cambridge: Cambridge University Press, 1993), pp. 74-92.

[21] B. Stocking, 'Factors affecting the diffusion of three kinds of medical technology in EC countries and Sweden', in S. Kirchberger, P. Durieux and B. Stocking, The diffusion of two

especial interest to this history, involving another type of research - epidemiology - are studies on occupational health, notably Weindling's collection.[22] This field is particularly relevant because a strong, somewhat unexpected theme which emerges from the present study is the construction at policy level of hepatitis B as an occupational hazard for health workers.

(ii) Work relating specifically to hepatitis B

As viral hepatitis became the subject of more intensive scientific investigation, an international scientific community grew up which by the 1970s reached the critical mass needed to launch major symposia; and the proceedings of these sometimes contain historical reviews.[23] Other, similar articles appeared in the journals.[24] Whilst these are useful

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technologies for renal stone treatments across Europe (London: King's Fund Centre, 1991), pp. 97-136; see also: B. Stocking (ed.), Expensive health technologies: regulatory and administrative mechanisms in Europe (Oxford: Oxford University Press, 1988)

[22] P. Weindling (ed.), The social history of occupational health (London: Croom Helm, 1985)

[23] S. Krugman, 'Perspectives on viral hepatitis infection: past, present and future', in G. Vyas, S. N. Cohen and R. Schmid (eds), Viral hepatitis: etiology, epidemiology, pathogenesis and prevention (Philadelphia: Franklin Institute Press, 1978; Tunbridge Wells: Abacus Press, 1979), pp. 3-10; R. H. Purcell, 'The hepatitis viruses: an overview and historical perspective', in W. Szmuness, H. J. Alter and J. E. Maynard (eds), Viral hepatitis: an international symposium (Philadelphia: Franklin Institute Press, 1982), pp. 3-12.

[24] S. Krugman, 'Viral hepatitis, overview and historical perspectives', Yale Journal of Biology and Medicine, 49 (1976), 199-203; R. H. Purcell, 'Hepatitis B: a scientific success story (almost)', Progress in Clinical and Biological Research, 182 (1985), 11-43.

for providing the bare outlines of the scientific advances made in the field, they provide minimal contextualization and little historical analysis. We learn from them that jaundice has been recognised since records began, that the viral nature of some hepatitis was speculated in the twentieth century, that during and after the Second World War two types of viral hepatitis were distinguished from one another - those now known as hepatitis A and B. A flurry of investigation following Blumberg's mid-1960s discovery of the 'Australia antigen' (which turned out to be part of the virus of hepatitis B) resulted in great strides in understanding the structure of the virus and the natural history of the disease. Relatively soon, a vaccine was developed.

All accounts emphasize the importance of the failure to grow the virus in a tissue culture, leading to the use of human volunteers for several early investigations. There has been controversy over this, but the literature does not make it clear who the attackers were. Later, primates and other animals were found to serve as experimental subjects. Genetic engineering facilitated further advances in experimentation and vaccine production.[25]

A useful and coherent account, though limited to a part of the scientific history, is provided by Baruch Blumberg, a key

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[25] P. Tiollais and M.-A. Buendia, 'Hepatitis B virus', Scientific American, 264, 4 (April 1991), 48-54.

participant.[26] He discusses some of the problems of gaining acceptance for testing blood donated to blood banks in the US, and the use of 'epidemiologic control alone' to control hepatitis in renal dialysis units. Here and in a joint paper,[27] he describes investigations which established sex differences in responses to hepatitis B, and the link between the virus and primary liver cancer. Worldwide mortality for primary cancer of the liver is estimated as several hundred thousand a year, making this the major international health problem associated with hepatitis B.

In the UK, outstanding hepatitis B investigator Arie Zuckerman has dominated the scene. His compilation of abstracts and summaries, the majority made by himself, gives a comprehensive view of scientific developments in the 1970s, and therefore deserves to be mentioned here although its contents are rather in the nature of primary sources.[28] What is clear from this book, as well as the two volumes Zuckerman has produced on viral hepatitis,[29] is that scientific papers and textbooks often fail to reflect policy concerns, even when the author is

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[26] B. S. Blumberg, 'The Australia antigen story' (Keynote Address) in I. Millman, T. K. Eisenstein and B. S. Blumberg (eds), Hepatitis B. The virus, the disease, the vaccine (New York: Plenum Publishing Corporation, 1984), pp. 5-31.

[27] W. T. London and B. S. Blumberg, 'Comments on the role of epidemiology in the investigation of hepatitis B virus', Epidemiologic Reviews, 7 (1985), 59-79.

[28] A. J. Zuckerman (ed.), A Decade of Viral Hepatitis (Amsterdam, New York, Oxford: Elsevier/North Holland Biomedical Press, 1980)

[29] A. J. Zuckerman and C. R. Howard, Hepatitis viruses of man (London, New York, etc: Academic Press, 1979); A. J. Zuckerman (ed.), Viral hepatitis and liver disease (New York: Alna R. Lise, 1988)

directly involved in policy formation as Zuckerman has been.

(b) Health policy

'Health policy' is a loose term, but writers such as Ham have clarified the processes by which health policy is formed, employing concepts which are broader than the history of the National Health Service (NHS) or the politics of health care.[30] Ham is concerned with the overall pattern of health service provision, with the dynamics of decision-making and implementation - or equally important, lack of decision or action. A central notion is the multiplicity of policy:

> policy may involve a web of decisions rather than one decision ... the actors who make decisions are rarely the same people as those responsible for implementation. A decision network, often of considerable complexity, may therefore be involved in producing action, and a web of decisions may form part of the network.[31]

Such a definition resonates with that offered in an analysis of health policy in Britain since the 1970s, which finds 'a complex web of mutual dependencies supporting a shifting assembly of pacts and bargains, both formally negotiated and tacitly understood'.[32] These open definitions, allowing for complexity, fit the broad scope aimed for in the present study. Unlike some more static definitions emerging from policy science, they emphasize the dynamic nature of the policy process, and the way that policies inevitably change

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[30] C. Ham, Health policy in Britain (Basingstoke: Macmillan, 2nd edition, 1985)

[31] Ibid, pp. 77-8.

[32] S. Harrison, D. J. Hunter and C. Pollitt, The dynamics of British health policy (London: Unwin Hyman, 1990), p. 2.

over time.

Ham employs the concept of 'policy community' first put forward by Richardson and Jordan to indicate the combination of that section of the central policy-making machinery responsible for a given issue, and the outside interests including pressure groups concerned with the same issue.[33] If we include in a putative hepatitis B 'policy community' the central agencies, regional health authorities, public health physicians, expert groups, and groups affected by hepatitis B - including gay men and a variety of health professions - there could be a veritable policy bedlam. In fact there has been comparatively little noise over hepatitis B, in the policy arena, and less in the press or public perception. This is a notable distinction from AIDS.

The hotly debated, much chronicled history of the National Health Service is generally concerned with the larger questions of health service organization and funding, rather than health policy making within the NHS on particular issues such as those discussed here.[34] But there are elements of

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[33] Ham, Health policy, p. 95, citing J. J. Richardson and A. G. Jordan, Governing under pressure (London: Martin Robertson, 1979)

[34] For a recent clash, see: Review and rejoinder: D. M. Fox, 'Anti-intellectual history?...', and C. Webster, '...Official history?', Social History of Medicine, 3,1 (April 1990), 101-05. This gives references to several histories of the NHS including the protagonists' own work: D. M. Fox, Health policies, health politics: the British and American experience, 1911-1965 (Princeton, NJ: Princeton University Press, 1986); C. Webster, Problems of health care: the National Health Service before 1957, Volume I of The health services since the war (London: Her Majesty's Stationery Office, 1988)

understanding provided by some of these histories that perhaps form a 'collective unconscious' background to the present study: the power of the organized medical profession; the view of successive governments that health was an illimitably expensive need which must somehow be rationed; the use of hierarchies and devolved responsibility to limit spending. Interestingly, although Klein introduces his study of the politics of the NHS with the assertion that 'this book is in no sense a history of the NHS', a historical approach is inherent in his analysis.[35] On the changing structures of the NHS, often confusing for the observer, Levitt's clarification of successive reorganizations is a helpful aid.[36]

The evolution of the welfare state - a broader subject than the NHS, with a longer history - is essential background to understanding postwar social policy including health policy; both Thane and Digby provide accessible texts, with Thane giving weight to political and economic factors and Digby bringing the story into the post-Beveridge era.[37] Lowe gives a detailed history of the postwar welfare state, with a brief history of the NHS among other sectors of welfare provison, and also provides a review of theoretical insights into the

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[35] R. Klein, The politics of the National Health Service (London and New York: Longman, 1983, 1989), p. vi.

[36] R. Levitt, The reorganised National Health Service (London: Croom Helm, 3rd edn. 1979); there is a more recent joint-authored edition covering further reorganization.

[37] P. Thane, The foundations of the welfare state (London and New York: Longman, 1982); A. Digby, British welfare policy: workhouse to workfare (London and Boston: Faber and Faber, 1989)

nature of policymaking.[38] Covering the whole period from the Victorian heyday of sanitary reform to the notion of local adviser and manager, Lewis shows the changing role of the public health doctor.[39] Community health physicians, or public health doctors, have been involved in dealing with hepatitis B 'in the community' because of their responsibility for infectious diseases.

The productive interplay between history and sociology of health is well reflected in Stacey's textbook, with its comparative perspective and generous bibliography.[40] A more anthropological analysis of lay concepts of disease, with the emphasis on the contemporary, is given in Currer and Stacey's collected volume.[41] Experiences of illness and of the health services are particularly well illuminated in Cornwell's study, based on interviews with families in the East End of London.[42] Problems of interviewing will be discussed presently in the section on sources; one of my regrets has been that my work did not involve more of Cornwell's 'ordinary people'.

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[38] R. Lowe, The welfare state in Britain since 1945 (Basingstoke: Macmillan, 1993), esp. pp. 39-61.

[39] J. Lewis, 'The origins and development of public health in the UK', in W. Holland, R. Detels and G. Knox (eds), The Oxford textbook of public health, 2nd edition (Oxford: Oxford University Press, 1991), pp. 23-33.

[40] M. Stacey, The sociology of health and healing (London and New York: Routledge, 1993; reprint of Unwin, 1988)

[41] C. Currer and M. Stacey (eds), Concepts of health, illness and disease (Leamington Spa, Hamburg and New York: Berg, 1986)

[42] J. Cornwell, Hard-earned lives: accounts of health and illness from east London (London and New York: Tavistock, 1984)

The wide ranging policy issues thrown up by hepatitis B in the UK have been scarcely discussed in the literature, in marked contrast with AIDS. A chronological outline of some policy issues was provided at an early stage by looking at official reports and circulars from the DHSS dealing with hepatitis B; these of course are primary sources for this study. More specific secondary sources are needed on areas of health policy relevant to hepatitis B: the blood supply, health workers in renal units, laboratories and other hepatitis-hazard settings, drugs, sexually transmitted diseases, gay health, the prison medical service and mental handicap institutions. Ideally, there would be a history of each of these with a clear exposition of policy changes over the past two decades, and plenty of references to hepatitis B in the index, but there is nothing like this available for any of the topics mentioned.

For the blood supply, there appears no recent study to rival Titmuss's 1970 policy study.[43] On drugs, MacGregor's collection refers to the 1980s but includes an historical paper,[44] while a paper by Robertson in a collection on AIDS and drugs refers to hepatitis B.[45] Sim's history of the

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[43] R. Titmuss, The gift relationship: from human blood to social policy (London: George Allen & Unwin, 1970)

[44] V. Berridge, 'Drugs: historical issues', in S. MacGregor (ed.), Drugs and British society: responses to a social problem in the 1980s (London and New York: Routledge, 1989), pp. 20-35.

[45] R. Robertson, 'The Edinburgh epidemic: a case study', in J. Strang and G. V. Stimson (eds), AIDS and drug misuse: the challenge for policy and practice in the 1990s (London: Routledge, 1990), pp. 95-107.

prison medical services provides a useful overview of a long timespan concluding with the present; although concentrating on the iniquities of the system, Sim misses the telling point that hepatitis B (like AIDS more recently) was prevalent in prisons.[46] Smith's study of the current crisis in the prison system links the high rate of drug taking by prisoners, both before entering prison and while incarcerated, with a supposed high incidence of hepatitis B (and AIDS): figures are hard to come by.[47] Mental retardation has received far less attention from historians of medicine than has mental illness; recent contributions stop short with the Second World War.[48] There is thus no secondary source which catalogues or explains the high incidence of hepatitis B in institutions for the mentally handicapped, a pattern noted by investigators from the Second World War onwards.

Despite the inclusion of 'sex' in the titles of many recent historical studies, there is really no British equivalent of Brandt's social history of venereal disease in the USA.[49] However, the wave of literature on AIDS has thrown up many studies which address such issues as attitudes to carriers,

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[46] J. Sim, Medical power in prisons: the prison medical service in England 1774-1989 (Milton Keynes and Philadelphia: Open University Press, 1990)

[47] R. Smith, Prison health care (London: British Medical Association, 1984)

[48] M. Thomson, 'The problem of mental deficiency in England and Wales, c. 1913-1946', D.Phil. thesis, University of Oxford, 1992; see also: J. W. Trent, Inventing the feeble mind. A history of mental retardation in the United States (Berkeley, Los Angeles and London: University of California Press, 1994)

[49] Brandt, No magic bullet.

segregation versus co-operation, testing and confidentiality, and health education - of relevance to hepatitis B as a sexually transmitted disease.[50] A review of some of this literature, placing it in its own historical context - of different phases in the response to AIDS during the first decade - is provided by Berridge and Strong.[51]

(c) The relationship between research and policy

As remarked earlier, the SSK literature on the production of scientific 'facts' is not generally concerned with policy. Historians have looked at ways in which science changed medicine from the mid-nineteenth century on: for instance, the contested ground of what constituted medical knowledge, to be included in a medical curriculum.[52] The incorporation of research into medical knowledge-formation can be compared with experimentalism in a wide range of scientific disciplines.[53] These sorts of studies help to locate medical research as part of the professional strategy of doctors, and to explain the

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[50] E. Fee and D. M. Fox (eds), AIDS: the burdens of history (Berkeley, Los Angeles and London: University of California Press, 1988); V. Berridge and P. Strong (eds), AIDS and contemporary history (Cambridge: Cambridge University Press, 1993)

[51] V. Berridge and P. Strong, Review Article: 'AIDS and the relevance of history', Social History of Medicine, 4 (1991), 129-38.

[52] C. Lawrence, 'Incommunicable knowledge: science, technology and the clinical art in Britain, 1850-1914', Journal of Contemporary History, 20 (1985), 503-20.

[53] J. V. Pickstone, 'Ways of knowing: towards a historical sociology of science, technology and medicine', British Journal for the History of Science, 26 (1993), 433-58; the four overlapping types of medicine discussed here are: biographical, analytical, experimental, and techno-medicine.

high prestige attached to certain types of research.[54] There are implications for policy on research, such as the slow take-off for clinical research in Britain between the wars.[55] However, this historical literature addresses the links between medical research and health policy only obliquely.

More overt concern with the links between research and policy can be found in policy science literature: a good starting-point is Klein's work (referred to earlier) which straddles the border between history and policy science. An absolutely fundamental concern here is what Klein defines as 'one of the main policy dilemmas faced by all modern societies: how best to integrate experts into the policy machinery' along with the workings of broader political processes.[56] Policy scientists have tended to focus on the role of social scientists and health professionals as experts, as in the work of Bulmer or Wistow.[57] American work offers a wider notion of science but warns that research often fails to make any impact on

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[54] On the wider issues of changing attitudes to medicine and its rising social value up to the interwar period, see: Lawrence, Medicine in the making of modern Britain.

[55] C. Booth, 'Clinical research', in Austoker and Bryder, Historical perspectives on the MRC, pp. 205-41.

[56] Klein, Politics of NHS, p. vi.

[57] M. Bulmer (ed.), Social science and social policy (London: Allen and Unwin, 1986), includes chapters by the author on: 'the policy process and the place in it of social research', and 'Types of research utilization: an overview'; G. Wistow, 'The health science policy community: professionals pre-eminent or under challenge?', in D. Marsh and R. Rhodes (eds), Policy networks in British government (Oxford: Clarendon Press, 1992).

policy;[58] research that is closely tied in with policy, while appearing more effective, is often fatally compromised.[59] Fox provides a rare review of historians as experts whose skills might feed into the policy process.[60]

It is one thing for research findings to be used by policy makers, and another for researchers themselves to become actors in policy making, as Berridge and Thom point out, in a paper which tests theories of the relationship between research and policy against their findings in case studies of policy on illicit drugs and alcohol.[61] Research does not simply inform policy in a direct fashion, through the force of evidence (the 'rational model'); rather it influences policy gradually, by diffusion through the networks or policy communities mentioned earlier (the 'enlightenment model'). In some instances of direct input, for instance when experts were called upon by the Department of Health to research the value of needle exchange schemes for addicts, research validates pre-existing policy agendas - in this case, a growing consensus for 'harm minimisation'. Berridge and Thom are discussing social science research here, and epidemiology and

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[58] D. Collingridge and C. Reeve, Science speaks to power: the role of experts in policy making (New York: St Martins Press, 1986)

[59] D. M. Fox, 'Health policy and the politics of research in the United States', Journal of Health Policy, Politics and Law, 15 (1990), 481-99.

[60] D. M. Fox, 'Review essay: Health and the care of sick strangers: Rosenberg, Stevens and the uses of history for health policy', Journal of Health Policy, Politics and Law, 16 (1991), 169-77.

[61] V. Berridge and B. Thom, 'Relationship between research and policy'.

statistics in relation to alcoholism; do their findings apply to the 'biomedical' research and epidemiology discussed in this thesis? Perhaps of particular importance is their identification of the powerful link between civil servants and medical experts as a 'policy community', almost separate from other interested parties.

For hepatitis B as for other diseases, we can expect to see a wide range of interpretations of current scientific evidence, and a variety of views on the best ways of implementing the latest understandings and technologies, all changing over time. The 'policy community' would include scientists, involved in research, who may actively inform policy making by sitting on advisory committees. Medical research may have been informed by policy needs, or divorced from them. Public funding of such research would arise partly from the perception of a public health problem, partly from the role of hepatitis B in the developing fields of virology and immunology, while commercial funding would be tied to the likelihood of profit from future sales of tests and vaccines. Moreover, medical research was one among a range of responses - preventive measures were an alternative focus for policy attention, or there could be a reluctance to act unless spurred on by political embarrassment.

(d) Literature relating directly to this study

The most important historiographical contribution so far in this field has been made by an American historian, William

Muraskin, looking at issues raised by hepatitis B in the US.[62] Muraskin's first paper introduces the evocative term 'The silent epidemic' to describe the lack of public attention given to this large-scale problem. He is making a contrast with the reaction to the epidemic of HIV/AIDS which shares many features with hepatitis B. However, in another memorable phrase, Muraskin calls hepatitis B 'the "Russian Roulette" of diseases' since its effects can vary from undetectable malaise to rapid death, or chronic and sometimes fatal illness.[63] Rather than use this variability as part of the explanation for the different response to hepatitis B and AIDS, Muraskin concludes that public health issues were suppressed in the case of hepatitis B because health workers form a significant risk group for this disease.

In a later paper, Muraskin argues that individual rights were placed above the public health interest, in the case of integration of mentally retarded children - many of whom would be hepatitis B carriers - into New York City schools in the late 1970s.[64] He comes to a similar conclusion in a further paper on the failure of adoption agencies and public health authorities to inform American families of the hepatitis B

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[62] W. Muraskin 'The silent epidemic: the social, ethical and medical problems surrounding the fight against hepatitis B', Journal of Social History, 22 (1988), 277-98.

[63] Ibid, p. 277.

[64] W. Muraskin, 'Individual rights versus the public health: the controversy over the integration of retarded hepatitis B carriers into the New York City public school system', Journal of the History of Medicine and Allied Sciences, 45 (1990), 64-98.

carrier status of Asian children they adopted.[65] Muraskin's approach veers towards conspiracy theory, and he tends to judge past actors rather as though they were up before a court. However, his accounts are fascinating, and his clearly delineated thesis on individual rights overwhelming the public health interest provides a springboard for thinking about issues like screening and vaccine policy.

There is little other historical work specifically on hepatitis. A particularly relevant conceptual history is offered in a paper by Ackerknecht on changing medical notions of the diseases now known as viral hepatitis, during the nineteenth and early twentieth centuries.[66] For the role that understandings of hepatitis B have played more recently, in relation to another disease, Oppenheimer's piece on the epidemiological construction of AIDS makes fascinating reading.[67] Reference has already been made to two papers published during preparation of this thesis; these have formed the basis for parts of Chapters 6 and 8 below.

In sum, most of the literature cited in this review provides broad context in terms of understanding the processes of

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[65] W. Muraskin, 'Individual rights vs the public health: the problem of Asian hepatitis B carriers in America', Social Science and Medicine, 36,3 (1993), 203-16.

[66] E. H. Ackerknecht, 'The vagaries of the notion of epidemic hepatitis or infectious jaundice', in L. G. Stevenson and R. P. Multhauf (eds), Medicine, science and culture (Baltimore: Johns Hopkins Press, 1968), pp. 3-16.

[67] G. M. Oppenheimer, 'In the eye of the storm: the epidemiological construction of AIDS', in Fee and Fox, AIDS: the burden of history, pp. 267-300.

medical research, of health policy making, and the relationship between these two. Because hepatitis B, like AIDS, is spread through blood, drug use and sexual contact, potentially a very wide range of secondary sources could be useful; however, there is a lack of histories of many of the services involved such as blood transfusion. Some of the scientific literature on hepatitis B can be used to form a narrative outline of 'discoveries', while policy documents enable a parallel framework of policy initiatives to be drawn up. For a coherent account and an understanding of issues raised by hepatitis B (selected issues, varying over time), detailed historical research was needed.

Sources

This study, located in the period from the middle of the Second World War up to the present, and dealing in most detail with the 1970s and 1980s, confronts the usual challenges of contemporary history:[68] lack of conventional archival sources, expectations from some quarters that the study will be oriented to future policy making, and the risk of offending actors personally involved in the history, whether they have been included as interview sources or not. Berridge has discussed these problems in relation to the history of health policy, pointing out that much of what we know about the past decade or so comes from other fields such as sociology,

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[68] For relevant commentary on the concept of contemporary history, see: V. Berridge and P. Strong, 'AIDS policies in the UK: contemporary history and the study of policy', Twentieth Century British History, 2 (1991), 150-74.

science policy, policy studies more generally or journalism.[69]

Certainly, I suspect, the reader of this thesis will notice a marked difference in density of information between the first chapter, which utilises material from the MRC archives, and all the rest. I asked for permission to use the Department of Health (DoH, formerly DHSS) archives and the MRC archives, now at Kew, for the post-1960 period with which the thesis is mainly concerned, but permission was refused. For this period, major primary sources have been articles in medical journals, policy documents, and interviews; in addition, I have used press cuttings, assorted material donated by interviewees, and other published material: obviously, certain books count as primary sources.

In fact one of the problems that I wrestled with in the early stages was how to categorise books and articles which seemed on the border between primary and secondary sources - this arose especially with very recent sources that were not obviously historiographical. The problem evaporated once I stopped making the distinction, listing them all in one bibliography. This may be unavoidable with contemporary history, and I think will be acceptable to other historians, as long as I have used a range of evidence to support my interpretations, rather than rely on the opinions of informants or journal authors.

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[69] Berridge, 'Health and medicine in the twentieth century', pp. 309-10, 313-14; see also: V. Berridge, 'Researching contemporary history: AIDS', History Workshop Journal, 38 (1994), 228-34.

Another important question for historians using medical journals is that of selection, which does not apply only to contemporary history, but perhaps is exacerbated by the enormous profusion of recent publications on a topic like hepatitis B (and of course the problem is a thousand times worse for AIDS). I began by looking for articles that had some bearing on policy; coming from an awareness of AIDS history, I looked particularly for papers which mentioned homosexuals or drug users. Then, as I built up a more rounded picture of my topic, I searched for articles on whichever part of the picture I was trying to clarify, for example hepatitis in haemophiliacs, or risks to laboratory workers. I acquired reprints from informants, on the science of hepatitis B more often than the policy. Since it was possible to read only a fraction of the - largely scientific - literature on hepatitis B, it seemed worth concentrating on the work of those I had interviewed; this approach yielded insights into the careers and types of work of selected researchers.

My outline of policy developments was built up from policy documents, loosely defined as documents having some official bearing on what was to be done with regard to hepatitis B in the health sphere.[70] I found most of the key DHSS reports quite early on, but compiling the various guidelines with a bearing on hepatitis B took longer. Current officials do not keep a complete set dating back twenty years, and the

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[70] For discussion of 'systems theory' in policy studies, see: Ham, Health policy, pp. 77-83: 'Outputs are essentially the decisions and the policies of the authorities' (p. 80) but there is also recognition of inaction, and of policies developing over time without formal announcements.

Department of Health library appears not to have a full listing either. In some cases, I was alerted by references in journal articles; in others, an informant provided a copy of guidelines I had not known about. DHSS documents appeared, until recently, to be very partial, with health workers figuring prominently, while drug users or gay men were relatively absent, an important finding about policy which was confirmed by other sources.

Documents relating to hepatitis B emanating from professional bodies or from local sources helped build up a more complex picture of the 'policy community' and the policy process. Examples include material on health and safety emanating from health and laboratory workers' unions; and papers loaned by a public health virologist reflecting local doctors' concerns over hepatitis B. Press cuttings from professional newspapers provided occasional illuminations of workers' worries, for instance over vaccination.

Clearly, interviews are another important source for such recent history; I have already referred to the way that informants supplied supplementary material, but the primary aim of the interview was to secure oral evidence. For the methodology of oral history, Thompson is the standard source, while Seldon and Pappworth discuss interviewing members of the 'elite'.[71] As with all interviewing, it was often difficult

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[71] P. Thompson, The voice of the past (Oxford: Oxford University Press, 1978; revised edition, 1988); A. Seldon and J. Pappworth, By word of mouth: elite oral history (London and New York: Methuen, 1983)

to separate the informants' memories of the recent past from their (current) interpretations; there is an additional level of difficulty attached where interviewees are high-powered doctors and scientists who have written a great deal on their subject, and may also have been involved in policy-making.

Another common difficulty with oral sources is informants' desire for confidentiality, which becomes particularly acute in sensitive areas of medical research and policy, especially for very recent periods. I understood this could be a problem for AIDS history, but I was surprised at the extent of the problem I faced in relation to hepatitis B history, with a high proportion (about a third) of informants declining to allow a tape recorder to be used. These tended to be people who were still working in the field, and they tended to be elite rather than 'shop floor' workers. Although some leading experts were willing to be recorded, they tended to retain tight control by insisting on previewing questions and allocating minimal time for the interview. Had I not already employed oral history methodology, I might have thought that my approach was faulty; but I had conducted forty to fifty interviews for a previous history of anaesthesia,[72] and had encountered only two refusals to have the interview taped.

The very recent nature of the study was clearly a factor in all this. Many informants were still at work, often stressed by their workload, and concerned about the repercussions of

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[72] J. Beinart, A history of the Nuffield Department of Anaesthetics, Oxford, 1937-1987 (Oxford: Oxford University Press, 1987)

giving information which then might be used in ways they had little control over. Retired people are often more willing to provide information without strings attached. But I sensed that beyond the usual factors, hepatitis B was a field riven with rivalries and littered with wounded professional sensibilities. It was also, clearly, at times seen as a dread or dirty disease, around which people had learned to tread carefully. The reason for not letting me see advisory committee minutes, according to the Department of Health, was that the issues discussed were still current - and very sensitive. There were times when the whole exercise seemed almost too difficult to carry through, but on the other hand, the lack of previous historical work on hepatitis B in this country was a great inducement to continue.

Outline

Chapter 2 traces major stages in scientific construction of hepatitis B which took place during and after the Second World War; prior to this time, there were very tenuous ideas about different types of hepatitis. Jaundice became important during the war on three main fronts: epidemics among troops, outbreaks associated with yellow fever vaccination, and cases following blood transfusion. Wartime work in Britain under an MRC Jaundice Committee, using volunteers, established that the commoner epidemic form (A) was transmitted via faeces.[73] The

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[73] F. O. MacCallum, A. M. McFarlan, J. A. R. Miles, M. R. Pollock and C. Wilson, Infective Hepatitis. Studies in East Anglia during the Period 1943-47, Special Report Series of Medical Research Council, no. 273 (London: HMSO, 1951)

terms hepatitis A and hepatitis B (for the blood-borne form, also seen after inoculation) were coined by this group. In the 1950s, Krugman in the US investigated the distinction between hepatitis A and B, experimenting on children in an institution for the mentally retarded.[74] The known high endemicity of hepatitis in such institutions was given as justification for these experiments, but their ethics were later questioned - an issue discussed in Chapter 2 in relation to both Krugman and the British wartime investigations. For the general theme of the thesis, insights into the workings of expert committees in this period are especially valuable.

Chapter 3 begins with an outline of postwar developments that form a backdrop for the history of hepatitis B after 1945, including new openings in clinical research. After a fairly quiet period, a major breakthrough in understanding hepatitis B came with Blumberg's mid-1960s identification of the 'Australia antigen', associated with the virus of hepatitis B; this American contribution is crucial.[75] From then on, testing for hepatitis B became a possibility, although early tests were not very sensitive and much effort went into improving their sensitivity and accuracy. Chapter 3 looks at the immediate impact of the Australia antigen discovery in the UK, where electron microscopy first revealed both the core structure of the virus and the viral particle itself. This brings the story up to 1970.

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[74] See: S. Krugman, 'Perspectives on viral hepatitis', pp. 6-7 for summary of findings of this research.

[75] B. S. Blumberg, 'The Australia antigen story'.

The next four chapters cover different themes within roughly the same timespan. Chapter 4 deals with a dramatic episode: between 1965 and 1972, outbreaks of hepatitis B in renal dialysis units introduced something of the 'shock of the new' to the picture.[76] With a few hundred cases up and down the British Isles, concentrated in ten of these units, the shock came not just from the spectacle of illness and death but from the fact that staff were frequently among the victims. Several informants spoke of the legacy of this period, comparing the fear inspired by hepatitis B at the time with that associated with AIDS fifteen years later. A relatively rapid and effective policy response came from an advisory group which in 1972 recommended exclusion of carriers of the Australia antigen.[77] Outbreaks in renal units ceased; the renal dialysis and transplantation programme was allowed to progress unhindered. Testing was not extended to other areas of the health service, other than to blood transfusion.

Chapter 5 looks at issues around hepatitis B in the blood supply. Prior to the Australia antigen discovery, the British system of unpaid donation was seen as superior, with respect to the rate of hepatitis in recipients, to that in countries

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[76] For comparable use of the term 'A shocking novelty' see: P. Strong and V. Berridge, 'No one knew anything: some issues in British AIDS policy', in P. Aggleton, P. Davies and G. Hart (eds), AIDS: individual, cultural and policy dimensions (Basingstoke: Falmer Press, 1990), p. 236.

[77] DHSS, Hepatitis and the treatment of chronic renal failure, Report of the Advisory Group, 1970-1972; Chairman: Lord Rosenheim (Department of Health and Social Security, Scottish Home and Health Department, Welsh Office, 1972) ['Rosenheim Report']

where blood donors were paid.[78] After the test for hepatitis B was applied throughout the blood transfusion service, from 1972,[79] the blood supply in the UK was regarded as extremely safe. There was no room for complacency. The major problem of hepatitis in the blood supply arose - in some ways reflecting the problem in renal units - from medical innovation, in this case the fractionation of clotting factors, mainly Factor VIII for haemophiliacs. As growing amounts of these products were supplied to haemophiliacs through the 1970s, many became infected with hepatitis B or non-A, non-B, although often without becoming overtly ill. In the interpretation offered in Chapter 5, the government's slow response to the request to make the UK self-sufficient in blood products is linked with the later infection of many haemophiliacs with HIV.

Chapter 6 explores research conducted through the 1970s. As the epidemiology was clarified, prevalence of hepatitis B was found to be high in Asia and Africa, moderate in eastern Europe and Latin America, and low in the more developed countries of the northern hemisphere. Hepatitis B was linked with primary cancer of the liver, an important cause of death in poor countries. The World Health Organization (WHO) worked to pool knowledge and ideas on means of control of

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[78] Titmuss, Gift Relationship.

[79] DHSS, Australia (hepatitis-associated) antigen, Revised report of the Advisory Group on testing for the presence of Australia (hepatitis-associated) antigen and its antibody. Chairman: W. d'A Maycock (Department of Health and Social Security, Welsh Office, 1972) ['Maycock Report']

hepatitis;[80] WHO policy may have helped gradually to shape national policy on hepatitis B, even in low-prevalence countries. In the UK, the hepatitis B test was the subject of intensive work in clinical, academic and pharmaceutical laboratories, with both public utility and private profit as motives. Aspects of the virology and immunology of hepatitis B were investigated, with difficulty since the virus would not grow in cultures. Chapter 6 studies a network of researchers in London: ways in which these scientists, doctors and technicians interacted are explored using notions of sample banks, and exchange of materials, summed up in the term 'blood brotherhood'. This analysis aims to bring an anthropological perspective to the question of how certain researchers come to be regarded as experts.

The construction of hepatitis B as an occupational disease is the heart of Chapter 7, together with questions of individual rights versus the public health interest. Laboratory workers afraid of losing their jobs without compensation succeeded in having hepatitis classified under industrial injuries legislation in 1975.[81] Accounts of practice in clinical laboratories suggest that safety measures were only gradually improved, and remained highly variable; codes of practice for

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[80] For example, with relevance to Europe: WHO, Viral Hepatitis, Report of a European Symposium convened by the World Health Organization, Prague, 29 Sept - 3 Oct 1964 (Copenhagen: WHO Regional Office for Europe, 1965); WHO, Viral Hepatitis, Report on a Working Group, Bucharest 25-29 Aug 1975 (Copenhagen: WHO Regional Office for Europe, 1976)

[81] DHSS, Viral Hepatitis, Report by Industrial Injuries Advisory Council in accordance with Section 141 of the Social Security Act 1975 on the question whether viral hepatitis should be prescribed under the Act (London: HMSO, 1975)

safety in laboratories became a battleground in the late 1970s. For many health workers, the chance of compensation was far outweighed by the fear of loss of livelihood if they contracted hepatitis B. The degree of concern varied, with dentists at the forefront.[82] But health workers, particularly surgeons, evidently wished to avoid compulsory screening, a position enshrined in 1981 DHSS guidelines on screening. The balance was set in favour of individual rights over public health; the role of expert advisers in formulating this policy is here examined.

The American vaccine against hepatitis B was available in the UK from 1982. Chapter 8 looks at the formation of vaccine policy, recognising that hepatitis B is a special case but at the same time relating it to other historical case studies. Since hepatitis B was seen as an occupational hazard for health workers, the vaccine might have been expected to provide the perfect public health solution: theoretically all new NHS staff, and those existing staff who were vulnerable, could have been protected from hepatitis. However, restricted guidelines persisted through the 1980s. The initial vaccine suffered from high cost and 'image' problems, but even when a cheaper recombinant (genetically engineered) vaccine with a cleaner image was introduced in 1987, the problem of cost still hindered delivery. Only one group other than health workers was strongly targetted for vaccination: that is babies

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[82] DHSS, Report of Expert Group on Hepatitis in Dentistry Department of Health and Social Security, Scottish Home and Health Department, Welsh Office (London: HMSO, 1979)

of mothers known to be carriers.[83] Delivery to the groups with highest prevalence - gay men and drug users - remained patchy. Chapter 8 explores the alliances for and against a broader vaccination policy, noting the possibility in the 1990s of a switch to universal childhood vaccination against hepatitis B.

Clearly some chapters focus more on research while others deal mainly with questions of policy: aspects of the relation between them emerge throughout. The policy focus on health workers and the enduring power of the medical hierarchy to influence policy, which have been identified by other writers, will be explored. The variable nature and locations of research - another theme raised elsewhere - will be used to explore networks of contacts and the making of experts. Interactions between initiatives at a local level and central policy making will also be highlighted. These and other aspects of the linkage, or lack of linkage, between research and policy on hepatitis B over a span of fifty years should have a bearing beyond this history.

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[83] S. Polakoff, 'Immunisation of infants at high risk of hepatitis B', British Medical Journal, 285 (1982), 1294-5.

CHAPTER 2: WARTIME DEVELOPMENTS: THE JAUNDICE COMMITTEE AND THE ETHICS OF HUMAN EXPERIMENTATION [Mainly 1942-1947]

This chapter focusses on work undertaken in Britain during the Second World War, which helped develop certain understandings of hepatitis A and B. First, previous changes in ideas about jaundice will be discussed in brief, with special attention to Ackerknecht's argument that the nature of infectious hepatitis was a subject of international scientific rivalry around the turn of the century. The mid-twentieth century notion that there was a form, or forms, of hepatitis caused by viral infection was contingent on the development of a concept of 'the virus', which will also be briefly reviewed. By 1942, hepatitis was seen as a hazard to troops, there were fears of spread to civilians, and urgent research was seen as the answer. A detailed account will be given of the wartime Jaundice Committee, particularly the contribution of the chief virological researcher and concerns raised by his experiments on human 'volunteers'. A growing recognition of hepatitis as a problem in blood transfusion was another outcome of wartime experience. Lastly, postwar hepatitis experiments in the US, which have generally received much more attention than the UK wartime experiments, raise interesting questions of changing ethical attitudes.

Concepts of hepatitis before the Second World War

Scientific papers on hepatitis which offer brief histories tend to delve into the ancient world and scan the whole of

history for references to jaundice, conveying little to the reader, beyond the fact that people have always noticed and linked illnesses which turn patients yellow.[1] Ackerknecht's review of medical ideas about hepatitis from the eighteenth to the mid-twentieth century is far more helpful, though marred by talk of 'improvements'.[2] It is surely more profitable to discuss past ideas in terms of 'understandings' rather than 'misunderstandings', to avoid separating the present 'us' with superior knowledge from the past 'them' with inferior knowledge - just as anthropologists gain greater insights by working from the interior meanings that social structures and rituals have for people practising them, than if they regard them as quaint and misguided customs.

Ackerknecht describes an influential nineteenth-century lobby, headed by German authorities (Virchow and Frerichs), supporting a non-infectious theory of jaundice.[3] The growth during the nineteenth century of chemically-induced liver disorders reinforced a research orientation towards toxins as a cause of acute cases of jaundice - Ackerknecht mentions phosphorus poisoning, an occupational disease, and we might add arsenic poisoning in venereal disease clinics in the early twentieth century. This orthodox view of acute hepatitis as a non-infectious condition was challenged towards the end of the

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[1] See Introduction, n. 23 and n. 24.

[2] E. H. Ackerknecht, 'The vagaries of the notion of epidemic hepatitis or infectious jaundice' in L. G. Stevenson and R. P. Multhauf (eds), Medicine, Science and Culture (Baltimore: Johns Hopkins Press, 1968), pp. 3-16.

[3] Ibid, pp.6-7.

nineteenth century by accounts of epidemics, first in military campaigns where epidemics of jaundice were witnessed, then in a factory and a mental institution where revaccination against smallpox seemed the common factor. The First World War and its aftermath saw reports of epidemics of jaundice multiply; Ackerknecht regards Germany's defeat in the war as contributing to the defeat of the old German notions about non-infectious jaundice, in favour of the views of French, Scandinavian, British and American physicians.

The concept of 'infectious jaundice' which was established by the interwar period tended to be unitary for many doctors, but those concerned with liver disease, with vaccination, or with the developing technology of blood transfusion, were becoming aware of a variant or variants, often associated with the use of needles and syringes, with a longer incubation period than the commoner epidemic form. By the Second World War, the terms 'infectious jaundice' or 'acute epidemic hepatitis' were in general use for the more common form, while 'homologous serum jaundice', 'arsphenamine' or 'arsenotherapy jaundice' and 'post-transfusion hepatitis' were used to indicate supposed variants arising in the peculiar circumstances of inoculation, injection or transfusion. These variations allowed room for continuing uncertainties over etiology, especially in the case of arsenic therapy, where the chemical was suspected of causing jaundice. But the notion that a virus could cause the disease was beginning to gain ground.

'The virus', virology and a viral etiology for hepatitis

The late nineteenth century had seen the emergence of Koch's postulates regarding the method of isolating a micro-organism from a diseased animal, plant, or person, and proving it caused a particular disease by reproducing that disease in another subject. The germ theory was shaken when it was shown that in the case of tobacco mosaic disease the infective agent could pass through a microbial filter. Either the germ theory was not universal for infectious diseases, and there were diseases caused by something akin to humours or miasmas, or else there must be sub-microscopic infectious agents which were far smaller than bacteria. Thus the concept of the virus around the turn of the century was, broadly speaking: a filterable disease-producing agent. Whether it fitted the definition of an 'organism' was (and still is) a matter of debate.[4]

While significant virus-oriented research in the interwar period centred on discoveries and debates on bacteriophage, a turning point came with further research relating to tobacco mosaic virus. As the historian Sally Smith Hughes puts it, the crystallization of tobacco mosaic virus by Stanley in 1935 changed the focus of virology from pathology to biochemistry, sparking off a whole new wave of investigations.[5] By 1950,

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[4] See: S. S. Hughes, The virus: a history of the concept (London and New York: Heinemann, 1977)

[5] Ibid, p.89, citing W. M. Stanley, 'Isolation of a crystalline protein possessing the properties of tobacco-mosaic virus', Science, 81 (1935), 644-45.

molecular biology and genetics were contributing to virology, with Watson and Crick's 1953 elucidation of the structure of DNA leading eventually to an explanation of the mode of reproduction of the virus within the host cell. Hughes points out that viruses have proved attractive to geneticists and molecular biologists because of their relative simplicity compared with the cell. Much progress in virology through the 1950s and 1960s was of a pure rather than applied nature, unravelling DNA and RNA rather than combatting viral infections.[6]

There appears to be a contradiction in Smith Hughes' periodisation, giving the mid-century as the point at which virology emerged as an independent discipline, since this is also the point at which it became definitively inter-disciplinary. Her argument hinges on the development of the concept of the virus, which reached a conjunction around 1950 that allowed more productive hypotheses to be formulated, with more interactive research deepening as well as broadening the field. Much research hinged on DNA; but much also arose from technological innovations such as tissue culture and electron microscopy. These general observations on virology in the postwar period are important for the next chapter.

But to return to the problem of hepatitis, and the tentative view that there was a viral etiology for at least some forms of jaundice. Papers published in 1937 and 1939 by Findlay and MacCallum exemplify the way that virology often worked at that

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[6] Ibid, p.102.

time, by a process of elimination.[7] They pointed out that for hepatitis, no micro-organism had been found which could be seen under a microscope, or trapped in a filter and cultured; therefore the causal agent presumably had to be a virus. Thus on the threshhold of the war, hepatitis was one among many diseases with 'candidate' viral etiology, but with the limited scientific tools at their disposal, it was not obvious how these virologists could hope to take matters further. In fact, they were concentrating on rather different problems which were to bring them back to hepatitis in an unexpected way.

MacCallum, Findlay, yellow fever vaccine and hepatitis

According to his own account, Fred MacCallum left Toronto for the UK in 1934 because he wanted to learn more about viruses, and resources were poor in Canada after the recession.[8] In Britain, he knew of three centres currently studying viruses: the Lister Institute, the Medical Research Council unit at Hampstead, and Findlay at the Wellcome Bureau of Scientific Research on the Euston Road, where the whole of the fourth floor was taken up with tropical medical research. Half the area was occupied by chemists working on antimalarials and

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[7] G. M. Findlay and F. O. MacCallum, 'Note on acute hepatitis and yellow fever immunisation', Transactions of the Royal Society of Tropical Medicine & Hygiene, 31 (1937), 297-308; G. M. Findlay, F. O. MacCallum and F. Murgatroyd, 'Observations bearing on the aetiology of infectious hepatitis (so called epidemic catarrhal jaundice)', Transactions of the Royal Society of Tropical Medicine & Hygiene, 32 (1939), 575-86.

[8] F. O. MacCallum, interview, 29 April 1992. Most of this section is based on this interview.

leishmaniasis, while Findlay worked alone on yellow fever, lymphogranuloma and rift valley fever. The Euston Road laboratories were the nexus of a chain reaching into Africa, with Wellcome's research laboratories in Khartoum and its mobile, floating laboratory on the Nile; and connecting with the laboratories at Beckenham in Kent, and others in the States, where drugs were manufactured.[9]

MacCallum originally took a job at the London Hospital under the professor of bacteriology, Professor Bedson, who had discovered psittacosis, but in July 1936 he secured a post as assistant to Findlay for research on yellow fever. They were experimenting with a vaccine, their Wellcome salaries subsidised by the Colonial Office which was concerned about yellow fever as a scourge of white officials and traders in West Africa. Others had long been searching for a vaccine, notably the Americans in relation to the building of the Panama Canal,[10] and Findlay collaborated with both the London School of Hygiene and Tropical Medicine (LSHTM) and the Rockefeller Foundation in New York, which had contact with South American ventures.

At this point - when MacCallum joined Findlay in 1936 - they were able to produce a live virus vaccine, manufactured from

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[9] A. R. Hall and B. A. Bembridge, Physic and philanthropy: a history of the Wellcome Trust 1936-1986 (Cambridge: Cambridge University Press, 1986)

[10] W. H. Wright, 40 years of tropical medicine research A history of the Gorgas Memorial Institute of Tropical and Preventive Medicine, Inc. and the Gorgas Memorial Laboratory (Washington: Reese Press for Gorgas Memorial Institute, 1970)

the brains of mice inoculated with infected serum. Passage through mouse brain was thought to attenuate the virus partially but not sufficiently for safety: to counteract any remaining virulence, large doses of serum from convalescent yellow fever patients were added to the freeze-dried mouse brain extract.[11] Later, it was found possible to grow the virus in chick embryos, a more satisfactory medium because more controllable. Rockefeller researchers found that after many passages through chick embryos, the virus vaccine was so attenuated that no anti-serum need be added; this vaccine proved satisfactory in trials conducted in Brazil in the 1940s.[12] However, although yellow fever vaccine had few precedents - it was the first virus vaccine for humans after smallpox and rabies - fixed ideas seem to have developed around it rather rapidly, and the notion that the freeze-dried vaccine must be made up with serum rather than water persisted right through the Second World War. This could be normal rather than convalescent serum, however.

Soon after MacCallum joined Findlay, cases of jaundice began to occur in people who had received yellow fever vaccine before going to Africa. MacCallum, still a new boy wrapped in notions of non-infectious jaundice, made little of this. Findlay was more concerned, and began to wonder about connections between this and other instances where jaundice followed injections. Together with MacCallum, he embarked on

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[11] Findlay and MacCallum, 'Note on acute hepatitis'; MacCallum, interview.

[12] Wright, 40 years of tropical medicine.

a literature search which revealed occasional cases of jaundice in various types of clinics - diabetes, arthritis, and others - in many different countries. They published on this phenomenon in 1937,[13] stating that their cases could not be yellow fever - the apparently obvious explanation in view of the colouration - since the jaundice occurred about sixty days after receiving the vaccine; moreover, blood samples taken from some patients established that thay had developed antibodies to yellow fever ten to fourteen days after inoculation. The findings pointed to hepatitis of a type analagous to that observed in the clinic cases they had surveyed.

Following this episode of 1936-7, Findlay and MacCallum had a clear period of about five years, providing yellow fever vaccines without further cases of jaundice. At the outbreak of war, Findlay was sent to West Africa as a tropical disease adviser, and MacCallum was left making yellow fever vaccine 'with a couple of technicians'. He was required to increase production from some twenty millilitres per week to several thousands, to provide for all service personnel going to West Africa.[14] Besides needing to increase the output of mouse brains, he believed he needed an enormously increased supply of serum for dilution of the vaccine. With what then seemed good fortune, a newly developed technology was available to channel large volumes of serum in a compact form: that is, freeze-dried plasma using pooled serum derived from many

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[13] Findlay and MacCallum, 'Note on acute hepatitis'.

[14] MacCallum, interview.

donors. The newly organised Blood Transfusion Service, set up in expectation of the war in 1938-9, relied heavily on freeze drying of blood and plasma, manufactured with the participation of the Wellcome company.

Thus when MacCallum was asked to step up yellow fever vaccine production, he called on a contact at Beckenham and secured a bottle of freeze dried plasma, which he reconstituted with water and incorporated into a batch of vaccine. Three months later, he was telephoned by the Director of the Royal Air Force medical services, who had suffered a nasty attack of jaundice sixty-six days after yellow fever inoculation.[15] This was one of several cases, the most severe in terms of seniority of the victim. MacCallum, knowing the batch number of the dried serum he had used, telephoned his Wellcome contact who still had some bottles of that same batch of plasma in store. These were used in some of the experiments that followed, instigated by the War Office.

The wartime Jaundice Committee and research team

As the war progressed, hepatitis became a cause of concern on a number of fronts. One the one hand, there were outbreaks of jaundice among troops stationed in the North African desert and in Italy - about 16,000 cases, with a few deaths, between 1941 and 1943, mostly ascribed to 'infectious hepatitis'.[16]

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[15] Ibid.

[16] 'Homologous serum jaundice', Memorandum prepared by Medical Officers of the Ministry of Health, Lancet, 1943, (i), 83-8.

On the other hand, outbreaks associated with yellow fever vaccine were an increasingly serious embarrassment. In the past, yellow fever had been a major impediment in the prosecution of military ventures in the tropics;[17] the vaccine was now seen as an essential safeguard. For a prophylactic measure to produce an illness, mimicking the disease it was designed to prevent, must have seemed an unfortunate mockery of the progress of British tropical medicine.[18] With America joining the war, there was a far more spectacular vaccine-associated jaundice outbreak: 28,000 US troops were affected in the first six months of 1942 (with 62 deaths), following inoculation with yellow fever vaccine made by the Rockefeller group, evidently still using serum to dilute the attenuated vaccine. The thousands of cases presented a frightening spectre of medically induced mass disablement.[19] When 500 American troops, newly arrived in Northern Ireland in 1942, suffered jaundice, the British became alarmed over possible spread to the civilian population.

As so often happened, the impact of war - in this case, an

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[17] P. Curtin, Death by migration: Europe's encounter with the tropical world in the nineteenth century (Cambridge: Cambridge University Press, 1988) surveys the stastistics, but shows how public health measures reduced yellow fever mortality long before vaccine was available.

[18] At this stage the British were feverishly stepping up production of synthetic anti-malarials, having been caught in the same trap of reliance on German manufactures they had experienced in the First World War, despite warnings in the interim. See: J. Beinart, 'The inner world of imperial sickness', in Austoker and Bryder, Historical perspectives on MRC, pp. 117-18, esp. 122.

[19] 'Jaundice following yellow fever vaccination' (Editorial), Journal of the American Medical Association, 119 (1942), 1110.

indirect impact, via a preventive health measure - acted as a stimulus to action on a medical front. It appears that the British and the US military agreed that research was needed to stem the flood of jaundice cases. Although there was an understanding that the US army was to investigate the yellow fever association, and the British to concentrate on infective heaptitis, in fact researchers on both sides of the Atlantic looked at every variant of hepatitis, since so little was known about it.

Sir Wilson Jameson, Chief Medical Officer at the Ministry of Health, asked the MRC to correlate existing research on jaundice and co-ordinate further investigations; a joint committee was established with MRC, armed forces and Ministry of Health representation. The Jaundice Committee met six times between March 1943 and May 1945, with a post-script gathering in October 1945 to settle its affairs. Clearly much negotiating was conducted before and between meetings; at the first meeting a research team was selected, with names already agreed upon, the only proviso being that the Wellcome Research Institute would have to be asked to release MacCallum for this work. A laboratory in the Department of Pathology at Cambridge was allocated for use by the research team, probably thanks to connections of one of the committee members.[20] The Ministry of Health was to make jaundice notifiable in Civil Defence Region 4 - that is, East Anglia and adjoining counties - to allow epidemiological surveillance of a normal civilian

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[20] This was Bedson, MacCallum's former boss, now serving on the Jaundice Committee, who was detailed to form the 'Jaundice Research Team'.

population of some two and a half million. All cases of jaundice among troops stationed in the area were to be closely monitoried by the research team. Already by the first meeting also, the use of 'human volunteers' for transmission experiments was under discussion.

Chair of the Jaundice Committee was Leslie Witts, Nuffield Professor of Medicine at Oxford; he was familiar with the field of haematology. Witts and Edward Mellanby, Secretary of the MRC, probably guided selection of committee members, though the other joint bodies (the forces and the Ministry) put forward their own men. A note from Witts to Mellanby late in 1943 reveals something of the personal element that must often have played a part:

> Poole [Major-General L. T. Poole, a medical supremo at the War Office, already on the Jaundice Committee] is very anxious that Biggam [another medical Major-General at the War Office] should be invited to become a member of the Jaundice Committee. Biggam is taking an active part in the Army's jaundice research and he is a person with whom I very much like working.[21]

Mellanby made sure that Biggam was invited. Members, as well as representing interested bodies - the Army, the Ministry of Health and the War Office - had to be eminent, known to the initiators, and, it would seem, compatible with the chairman. Almost all were London-based except Witts in Oxford and W. J. Tulloch, Professor of Bacteriology at St Andrew's - and A. M. McFarlan, an epidemiologist at the Emergency Public Health Laboratory at Cambridge who acted as Secretary to the Jaundice Committee and was also a member of the research team.

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[21] MRC 3217/1, Jaundice, increase in the incidence. Committee, constitution & members, L. Witts to E. Mellanby, 4 Oct 1943.

Each of the five members of the research team covered a particular aspect. McFarlan, seconded from the Public Health Laboratory Service (PHLS), conducted the epidemiological surveys. Clifford Wilson, a senior Army physician, undertook clinical observations. M. R. Pollock, a bacteriologist from the PHLS, dealt with the biochemical problems of early detection of infective hepatitis (prior to onset of jaundice), and assessment of liver function in relation to different treatments. J. A. R. Miles, a clinical pathologist from the Army, conducted haematological and serological investigations. Transmission experiments were the responsibility of MacCallum. The following account will concentrate mainly on the latter, and on the role of the Jaundice Committee in facilitating, sanctioning, and 'image-managing' these experiments.

It appears from the final report of the research team as if MacCallum initially concentrated on finding an animal model, but in fact he had already done this work before the Jaundice Committee was established, as he reported to an MRC sub-committee on Jaundice in Industry in November 1942.[22] Noting the almost totally unsuccessful work of other researchers, he had tried pigs, golden hamsters, Orkney voles, cotton rats, guinea pigs, canaries, mice, and rats, all with negative results. The failure of these earlier attempts to find an animal in which hepatitis could be produced, led the Jaundice Committee to support MacCallum's call to use human beings as experimental subjects:

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[22] MRC 3217/4, Jaundice in Industry, 'Hepatitis Sub-Committee', minutes of meeting at LSHTM, 20 Nov 1942.

> It was decided, therefore, that experiments on human volunteers were essential if further knowledge was to be obtained on the mode of spread and duration of infectivity of the various types of hepatitis designated as infectious, homologous serum and arsenotherapy hepatitis.[23]

How were volunteers obtained? The first line was to try conscientious objectors; MacCallum 'went to talk to Quakers in that building [the Friends' Meeting House] next to the Wellcome Institute on the Euston Road' and persuaded 'first one then another' to participate. This source was not plentiful enough, however; soon 'there weren't any more conchies' willing to act as experimental subjects.[24] Dr W. H. Bradley, a Ministry of Health appointee on the Jaundice Committee, suggested that rheumatoid arthritis patients might be recruited, on the basis of reports in the prewar literature, suggesting an attack of jaundice sometimes brought about remission of arthritis symptoms.[25]

Witts leaned on rheumatology colleagues and secured a group of volunteers in a unit in London, for what was billed as a therapeutic trial of the effects of jaundice on rheumatoid arthritis. Witts used the term 'inoculation' of the procedure used in these trials, but MacCallum describes various methods of administering the infected material - nasopharyngeal

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[23] MacCallum et al, Infective hepatitis, p.117.

[24] MacCallum, interview.

[25] Bradley cited (incompletely): G. F. Still, 'On a form of chronic joint disease in children, Transactions of the Royal Medical-chirugical Society, 80 (1897), 52, where only passing mention is made of this effect; and the much fuller account in: P. S. Hench, 'Effect of jaundice on chronic infectious (atrophic) arthritis and on primary fibrositis', Archives of Internal Medicine, 61 (1938), 451-80.

washings, blood, urine or faeces from hepatitis patients - including spraying into the nose and mouth, swallowing, and injection. In the case of faeces, which (from delicacy of feeling) MacCallum left till last, a suspension in orangeade was apparently most favoured among the recipients.[26] Infective material was derived from Wilson's patients, mostly service personnel in East Anglia (for infectious hepatitis); and from cases of post transfusion hepatitis supplied by the Blood Transfusion Service.[27]

By March 1944 a fresh supply of volunteers was needed, for further transmission experiments; the Jaundice Committee decided to request the use of military prisoners both in the Middle East and in the UK, and also civilian prisoners. Witts asked Mellanby to contact the civil and army authorities, and provided him with a persuasive case, including statistics which appear, in retrospect, rather chilling:

> The risk of fatality is probably no greater than is represented by a fatality rate of 8 in 10,000 cases in the recent epidemics in the Middle East. The risk of subsequent disability is probably about 1 per cent of cases. These rates of mortality and disablity apply to individuals actually contracting infective hepatitis, and

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[26] MacCallum, interview: military colleagues advised first investigating faeces, as the most likely means of transmission of infectious hepatitis, but MacCallum prioritised the views of a Yorkshire GP who thought the disease might be carried by airborne particles; see: W. N. Pickles, Epidemiology in country practice (Bristol: Wright, 1939). Faecal material was treated by centrifugation and ether extraction or freeze-drying, then disguised with vanilla or suspended in orangeade, before use; see: MacCallum et al, Infective hepatitis, p. 119.

[27] F. O. MacCallum and J. D. Bauer, 'Homologous serum jaundice. Transmission experiments with human volunteers', Lancet, 1944 (i), 622-7. See also: MacCallum et al, Infective hepatitis, p.127 for reference to pool of serum identified as source of jaundice; this Batch 034 was made from serum from 1000 'supposedly normal' donors at blood banks.

> these would be only a small fraction of the total number of volunteers inoculated.[28]

Witts speculated that men who were serving sentences for desertion or cowardice might 'welcome this means of rehabilitating themselves in the eyes of society', that civilian prisoners would like to contribute to the war effort, and that all would welcome remission of their sentences. But the prisoners were never subjected to this tempting offer, since the Adjutant-General ruled that the need for six months observation of experimental subjects might hamper remission for military prisoners who were in for short sentences. Besides, as Lieutenant-General Sir Alexander Hood, Director-General of the Royal Army Medical Corps added, in relaying the decision to Mellanby:

> Though the risk of fatality is exceedingly low, there might well be a death in the earlier stages of the experiments, and this might easily lead to very considerable trouble.[29]

Mellanby drew a similar blank with his request to the Prison Commissioner for the use of civilian prisoners, on the grounds that additional remission (above that normally allowed for good behaviour) would not be acceptable to the Home Office.[30]

Refused the use of prisoners, and seeing problems with other possible groups which they discussed (such as inmates of lunatic asylums and monastic orders), the Jaundice Committee pressed ahead with a search for further pools of rheumatoid

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[28] MRC 3217/8, Jaundice - Transmission to volunteers, L. Witts to E. Mellanby, 24 March 1944

[29] MRC 3217/8, A. Hood to E. Mellanby, 25 May 1944

[30] MRC 3217/8, Dr Methven, Prison Commissioner, to E. Mellanby, 10 May 1944.

arthritis patients. A letter to The Lancet was drawn up over the signatures of Bradley and MacCallum, on the beneficial effects such patients sometimes experienced with jaundice. As Witts confided to Landsborough Thomson, second secretary to the MRC, in July 1944, one of Bradley's superiors at the Ministry of Health was 'very worried about his connection with this work and raised very strong objections to publication unless it had the declared support of the Council'.[31] The requisite support for publication was secured, with the assurance that the Jaundice Committee fully recommended it. Their grounds for so doing were partly that transmission experiments had already shown that the faeces of patients with infective hepatitis contained an infectious agent - a finding of great practical importance - and partly the desire to establish Bradley's priority with regard to this transmission and the use of the infectious agent in treating rheumatoid arthritis patients. After this, Bradley was no longer to be closely associated with transmission experiments.

The Ministry of Health perhaps had additional reason to be wary of their man's name being associated with further experiments; the Ministry itself had requested the Jaundice Committee to look into what was termed 'homologous serum jaundice' in the context of transfusions of blood and serum. Bradley told a Jaundice Committee meeting in July 1944 that:

> ... the Ministry of Health had records of 200 cases of hepatitis in transfused persons with 5 deaths ... The Ministry was concerned about the possibility of public

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[31] MRC 3217/8, L. Witts to A. Landsborough Thomson, 17 July 1944. By 'support of the Council [the MRC]', Witts meant the support of Mellanby.

> clamour if it became known that many cases of jaundice and some fatalities were due to transfusion.[32]

Most of these cases had been reported by doctors J. F. Loutit and Janet Vaughan, both of whom attended this meeting;[33] the latter requested a full time social worker to assist her search for further information on the links between blood transfusion and jaundice, which the MRC agreed to fund.

To those involved with the transmission experiments, it was now clear that further trials would not be limited to the less harmful infectious jaundice, but would include serum jaundice. To this was added a third variant, representing what MacCallum referred to as the 'social aspects' of the disease;[34] that is, jaundice associated with the arsenical treatment of venereal diseases: arsenotherapy or arsphenamine jaundice. The theory that this type of jaundice arose as a side-effect of the arsenical drugs had survived from the original cases until well into the 1940s, but the prevalence of jaundice in venereal disease clinics attended by Italian prisoners of war had worried the military doctors and led to some suspicion that an infectious agent might be responsible - something that was inadvertently transmitted via needles and syringes.

By September 1944, Witts had taken steps to facilitate the new round of experiments, as he told Mellanby:

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[32] MRC MB39, Jaundice Committee Minutes, Minutes of fourth meeting, held at LSHTM, 11 July 1944.

[33] Dr Janet Vaughan sat on the Transfusion Hepatitis sub-committee of the MRC Blood Transfusion Research Committee.

[34] MacCallum, interview.

> We have provided 58 patients with rheumatoid arthritis for MacCallum to inoculate here in Oxford. Although I say 'we', my Assistant Director, Dr Alice Stewart has made all the arrangements.[35]

These arrangements included the opportunity to draw on patients at another centre, as Witts explained:

> Dr Alice Stewart is the daughter of Naish, Emeritus Professor of Medicine at Sheffield, and she has a number of connections there. We have made tentative enquiries and it would be possible for us to work up the Sheffield area and collect at least 100 volunteers with arthritis, probably more.[36]

Oxford and Sheffield were the main centres for the human transmission experiments which now included several different types of jaundice; but other cases were 'made available' in several hospitals in Scotland, Wales and elsewhere in England.

Sensitivity on the part of hospital authorities to the possible public view of these transmission experiments emerges in a couple of instances. The medical superintendant of Aberdeen Royal Infirmary, Dr J. C. Knox, wrote directly to Mellanby, pointing out that a voluntary hospital which was:

> very dependent on public trust and goodwill for its financial support cannot afford any suggestion that patients, even volunteer patients, are being 'experimented' upon ...[37]

Mellanby, after referring the question to members of the research team in Cambridge (MacCallum and McFarlan), assured Knox that the risk to his arthritis patients from jaundice therapy was no greater than with gold therapy, another more favoured experimental treatment, and advised that he emphasize

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[35] MRC 3217/8, L. Witts to E. Mellanby, 29 September 1944.

[36] Ibid.

[37] MRC 3217/8, J. C. Knox to E. Mellanby, 11 February, 1944.

this therapeutic aspect to the hospital's Board of Governors. But Mellanby also stressed the question of the national interest: jaundice research was 'of high priority in relation to the war'.[38] A further instance of potential for objections from the hospital authorities will be discussed below, in relation to the final stages of the research team's findings.

MacCallum's typical weekly schedule during the peak period of transmission experiments was fairly hectic.[39] He spent Monday mornings at the Wellcome laboratories in the Euston Road, where he was still making yellow fever vaccine, with a medical conscientious objector as assistant. On Monday afternoons he went up to the headquarters of the jaundice research group in Cambridge, to coordinate the team's work (and perhaps collect clinical material). He would spend Tuesday and Wednesday in Sheffield conducting transmission experiments on volunteer arthritis patients, and then return to Cambridge on Thursday to monitor the progress of his animal experiments. Friday would be spent back in London. Meanwhile, McFarlan was working in East Anglia, looking at outbreaks of hepatitis in schools, nurseries, and a large institution for mental defectives where there were 85 cases of 'infective hepatitis' in an outbreak in 1944.[40] Wilson was in Cambridge making

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[38] E. Mellanby to J. C. Knox, 28 February 1944.

[39] MacCallum, interview. Note that he refers to animal experiments; in this recollection, nearly fifty years after the event, these were continuing alongside the human transmission experiments. This may indeed have been the case even though it is not evident from the published or archival sources.

[40] MacCallum et al, Infective hepatitis, p. 37.

clinical observations on patients - three hundred of the two thousand servicemen in the region notified as cases of infective hepatitis - while Pollock developed biochemical tests for early detection of infective hepatitis and changes in liver function. Miles, also at the jaundice research team's headquarters, worked on haematological and serological reactions to clarify the clinical profile and distinguish the different types of hepatitis.

Towards the end of the war (and of the Jaundice Committee's activities), there was further cause for alarm over potential objections to the transmission experiments, and this time there is evidence of deliberate evasion. MacCallum had been publishing his findings in a series of articles, each of which had first to be submitted to the Jaundice Committee for approval. The last in the series dealt with arsenotherapy jaundice, which appeared to be transmitted by blood, but not by faeces and nasal washings. This was an important finding but there was a problem, as MacCallum had to confess to Mellanby:

> I had included Dr Alice Stewart's name, as we had done the work together, but as you will see she has erased this, as she felt the situation in Sheffield would be happier if the clinic did not realise that material from patients receiving arsenotherapy had been inoculated into their patients.[41]

The real problem, which MacCallum avoided spelling out, was a fear of possible syphilis transmission alongside hepatitis, since arsenic therapy was used for treatment of syphilis. MacCallum was confident that his methods ensured that the

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[41] MRC 3217/8, F. O. MacCallum to E. Mellanby, 7 March 1945.

material he used would carry only hepatitis, not syphilis, but there could be little doubt that this part of the trials was potentially very controversial.

MacCallum's experiments using material from two patients who had become jaundiced during arsenical treatment, with nineteen volunteers as recipients, confirmed the view that an infective agent carried from one patient to another via needles and syringes might be responsible for so-called 'arsenotherpay jaundice', rather than the arsenic itself. The infective agent appeared to be the same as for serum hepatitis (as in the cases of vaccine and transfusion hepatitis). The findings also indicated that better sterilization of needles and syringes could stop transmission.[42] These were important advances. But Witts well understood Alice Stewart's refusal to associate her name with the work - as he told Mellanby:

> I have been on tenterhooks about this work, as it has been carried out in patients with rheumatoid arthritis under the guise of homologous serum jaundice ... I have become increasingly uneasy about the issue raised [of possible transmission of syphilis] ... At the meeting in December ... I got the Jaundice Committee to give a ruling that experiments on the transmission of post-arsenical jaundice must not be carried out on patients with rheumatoid arthritis, and I believe that no further experiments of this kind have been performed since that date ... I am hopeful that this is the last hurdle which the Jaundice Team faces. I must confess that this study of human transmission has caused me a good deal of worry and it is a great relief that no permanent ill effects have been observed in any of our volunteers.[43]

Whether by permanent ill-effects he meant syphilis or

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[42] MacCallum et al, Infective hepatitis, p. 134; MacCallum, interview: in a large and busy Army clinic syringes thrown into the autoclave and removed at random might not stay in for the requisite 10 mins; Army informants confirmed the presence of minute quantities of blood in the needles/syringes.

[43] MRC 3217/8, L. Witts to E. Mellanby, 7 March 1945.

hepatitis, Witts could indeed count himself lucky that no patients showed lasting damage - and that there were no deaths from the more serious serum hepatitis. (The question of patients suffering sub-clinical infections leading to a carrier state would not arise at this time.) Mellanby, acceding to Witts' request for clearance of MacCallum's article, without recourse to the Jaundice Committee, commented that 'publication certainly has my approval and, although some people might regard it as strong meat, I realise that it is the kind of work that had to be done.' Shortly afterwards, MacCallum was moved to typhus research and the Cambridge jaundice team was dispersed.

The final report of the research team was published in 1951, some four years after the last recordings were made; in its preamble, it was stated that the MRC decided not to prioritise publication because many of the findings had been published during the course of the investigations, and other reports now took first turn.[44] But this seems an inadequate explanation; it seems reasonable to suppose that the delay may in part have been occasioned by the nervousness so eloquently displayed in the Jaundice Committee files.

The broad scope of the enquiries, and the various prior classifications of types of jaundice, led to a wide ranging

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[44] Preface to MacCallum et al, Infective hepatitis, p. iii; authorship of the Preface is not given; it is dated 4 Sept 1951, and states that: 'The investigation recorded here ended in 1947 and the report in its present form was accepted for publication not long afterwards', but was then postponed to make way for other reports; it was published unrevised despite further knowledge on hepatitis accumulated meanwhile.

series of conclusions, among which the major distinction between two types of hepatitis does not always stand out. For instance, under the summary findings for serology: 'The evidence suggested a different causation for infective hepatitis from that of homologous serum or arsenotherapy hepatitis, but there is no evidence for or against cross-immunity between the latter two conditions'.[45] In discussion of transmission experiments, a new term was introduced:

> Infective hepatitis is believed to be due to a virus called virus A ... Virus B causing homologous serum hepatitis has not been found in faeces ... the derivation of virus B and its possible relation to virus A remains undecided.[46]

Would it be reading backwards to see the distinction between hepatitis A and B as the most important achievement of the Jaundice Team? The same point was stressed in the MRC's preface to the report, without using the terms 'A' and 'B':

> The outstanding findings of the human experiments were that a virus is present in the blood in arsenotherapy jaundice and that virus is excreted in the faeces in infective hepatitis.[47]

A wider audience had probably been reached, however, through journal articles, possibly the most crucial being one written by MacCallum but appearing anonymously in The Lancet in 1947.[48] Here, the suggestion was clearly made for the first time that the disease with a short incubation period (20-40 days), known as catarrhal jaundice or infectious or infective hepatitis be called hepatitis A, while the disease with a long

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[45] MacCallum et al, Infective hepatitis, p. 143.

[46] Ibid, p. 144.

[47] Ibid, p. iii.

[48] 'Homologous serum hepatitis' (Editorial), Lancet, 1947 (ii), 691-2.

incubation period (60-100 days), known as homologous serum jaundice, be called hepatitis B.

Very much remained a mystery regarding the nature of hepatitis B, and its epidemiology was far more obscure than that of A. MacCallum thought the high attack rate among his experimental subjects, inoculated with B, suggested that 'only a small proportion of the population has been exposed to this agent as compared to virus A in England'.[49] Perhaps this was a new disease, he speculated, or was natural transmission extremely difficult? The apparent increase in cases over the years might be due to better recognition, or to an actual increase due to the more widespread use of blood products. There was even a possibility of interaction between viruses, as there seemed to be some evidence that individuals who had recovered from B were more susceptible to A than normal.

We can see in this sort of speculation an image of hepatitis B as a rare, possibly new, disease, chiefly associated with medical procedures involving blood, serum or plasma. The virus had been found to be tough, yet the disease apparently failed to spread widely where there was no puncture of the skin by needle: it was not transmitted by the faecal-oral route like hepatitis A, nor by droplet infection like so many other infectious diseases. Buried in the MRC report, in McFarlan's discussion of two outbreaks of hepatitis in a mental institution, was a possible clue; he referred to both types of hepatitis (the prior outbreak was supposed to be B,

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[49] MacCallum et al, Infective hepatitis, p. 138.

and the one he studied in 1944, to be A) as having spread partly through 'contact'.[50] While McFarlan emphasized the uncleanly habits of the 'low-grade' inmates in relation to the spread of infective hepatitis,[51] the pattern of spread among people living in close proximity echoed that observed in families in the villages he had studied.[52] Further, postwar studies in a mental institution in the US were further to elucidate the nature of the transmission routes and the meaning of 'contact'.

Wartime work on post-transfusion hepatitis

During the war, the MRC ran a blood transfusion research committee to tackle problems arising from wartime expansion of the blood transfusion programme. In 1942/3 it set up a sub-committee on hepatitis, mainly because of the hazard associated with serum and plasma: measles convalescent serum, yellow fever vaccine containg human serum, and transfusion of pooled plasma for peripheral vascular disease. At this point, 'only few cases of hepatitis have been noted following transfusion',[53] but this was almost undoubtedly due to follow-up difficulties. Janet Vaughan submitted a memorandum on post-transfusion hepatitis, and the committee agreed to initiate a survey of Emergency Medical Service hospitals to

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[50] Ibid, pp. 37-45.

[51] Ibid, p. 43.

[52] Ibid, pp. 27-33.

[53] MRC 2181/10g/2 Jaundice following transfusion, MRC blood transfusion research committee. Sub-committee on hepatitis following transfusion (Draft circular, no date, probably 1943)

uncover the extent of the problem.[54]

Two immediate questions arise. Why did not the Ministry of Health make jaundice notifiable, to facilitate collection of data? This was discussed in August 1942 at a special meeting on jaundice associated with homologous serum (eg measles or mumps serum), where Professor Arthur Ellis of the MRC asked why the Ministry had decided against making jaundice notifiable. Dr J. R. Hutchinson from the Ministry explained the basis for the decision, and 'the meeting then did not press for notification' - but Dr Hutchinson's reasons are not recorded in the minutes.[55] One can only guess, that in the fraught conditions of wartime, the Ministry wished to avoid the risk of a nationwide scare over vaccine programmes which had resulted in hepatitis deaths. Limited notification was an alternative, as in the East Anglia region for the Jaundice Committee's research, or the proposed reporting of post-transfusion jaundice from selected hospitals.

A second question arises over the organization of research: why should the MRC, rather than the Ministry, organize collection of data requiring routine transfusion follow-up? This happily is fully answered, in a passage which gives a

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[54] Ibid, Minutes of second meeting, Thurs 28 July [1945]; Dr Vaughan's work is also mentioned in same file, Committee on Jaundice, Minutes of fifth meeting, 7 Dec 1944: 'Dr Janet Vaughan had obtained the services of a whole-time social worker, Miss N. Spurling, to follow up patients who had been transfused'.

[55] MRC 2181/10g/2, Jaundice following administration of homologous serum, Note of informal meeting, 13 August 1942; the Army Blood Supply Depot, the US Army, the Emergency Blood Supply, the MRC and the Ministry of Health were represented.

frank MRC view of the Ministry's shortcomings with regard to research:

> ...there was general agreement that this was a research problem, and could only satisfactorily be tackled by some ad hoc organization best run by the MRC. If it were run by the Ministry a host of officials would be involved and there would be little hope of satisfactory contact or co-ordination.[56]

The chief result was to be a six-monthly report on hepatitis following transfusion of blood or plasma in selected regions. Although relating specifically to hepatitis, the view of the respective abilities of the MRC and MoH for data collection recorded here presumably applied much more widely.

The question of whether or not to exclude donors with a history of jaundice from giving blood received perfunctory discussion at this point. A rapid survey was undertaken, within one of the committees: 'A third of the committee had a history of jaundice at one time or another and if this were a picture of the entire population donor panels would be seriously affected by omitting those with a history of jaundice.'[57] It may be fortunate that not all MRC research was conducted in so cavalier a fashion.

Clearer details of the findings on post transfusion hepatitis appear in a summary supplied in April, 1946, by Witts, chair of the Jaundice Committee. Witts pointed out that only late in the war was the danger of plasma jaundice noted. He quoted

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[56] MRC 2181/10g/2 MRC sub-committee on transfusion hepatitis, second meeting, 28 July [1945].

[57] MRC 2181/10a Blood transfusion - Research problems - General VI, Blood transfusion research committee, ninth meeting, 6 Nov 1942.

Janet Vaughan's suggestion that most plasma pools caused one to two per cent post transfusion hepatitis, but some caused far more; her own follow-up survey had given a rate of 7.3 per cent. In a study under the Jaundice Committee, of over 1,000 injured, transfused patients kept under observation for three months or more, 124 developed hepatitis, which proved fatal in 17 cases, a rate of 9.4 per cent.[58]

Until late 1944, policy on plasma production had been to pool at least 100 litres of plasma from about 500 donors, giving 250 bottles of the final product; but from March 1945, in the light of the findings outlined, the pool size was reduced to 10 bottles per batch.[59] Accumulated evidence was pointing towards large pools as the culprit in major incidents of serum hepatitis transmission, and the lesson was learned and applied before handing the transfusion service over to the NHS.[60] Postwar developments in the blood transfusion service will be outlined in the next chapter, while issues of hepatitis B in the blood supply will be explored in Chapter 5. However, it is appropriate to discuss here a contentious series of postwar hepatitis experiments carried out on children in a mental deficiency institution in the US, in order to make comparisons

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[58] MRC 2181/10g/2 Jaundice following transfusion MRC sub-committee on transfusion hepatitis, second meeting, 28 July [1945], addendum 3: J. C. 24, Table of results of search of Ministry of Health's statistical branch at Norcross of Emergency Medical Service hospital records of 1940-45 inpatients.

[59] Presumably this means 10 donations.

[60] MRC 2181/10g/2 Jaundice following transfusion MRC sub-committee on transfusion hepatitis, letter from L. J. Witts to A. Janeway, Harvard Medical School, 25 April 1946, quoting JC24, table of results of search of MoH statistical branch.

with MacCallum's UK wartime experiments.

Postwar experiments on hepatitis: Krugman's Willowbrook studies

The hepatitis experiments carried out by Saul Krugman between 1956 and 1971 subsequently received both high commendation and (to a much greater extent) deep opprobrium; but at the time they started, they appear to have been fairly uncontroversial. Krugman was a New York paediatrician, with a post from 1946 in the Department of Pediatrics at New York University, where he worked with colleagues on infectious diseases of children, particularly measles and rubella. His interest expanded to hepatitis and in 1956, together with Joan Giles and Jack Hammond, he began a series of studies in Willowbrook, a residential school on Staten Island in New York, housing about five thousand mentally defective children between the ages of three and ten years old. Within this institution - as in many such institutions for the mentally deficient - viral hepatitis appeared to be common, and Krugman's team sought to elucidate the type of hepatitis involved, and the means of transmission, by adminstering infective material to newly-admitted children. A special hepatitis unit was established in the school and children whose parents agreed to submit them to the trials were given faecal material or serum from hepatitis sufferers, in drinks or by injection.[61]

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[61] Parental permission was crucial, but was given on a general understanding of the nature of the experiments rather than detailed protocol; as with MacCallum's experiments, the exact nature of the material used for transmission trials was not spelled out to subjects.

Fifteen years of experiments on several hundred children at Willowbrook resulted in many papers, published in leading American medical journals, and wide acclaim for Krugman's achievements.[62] However, the Willowbrook trials came under increasingly hostile scrutiny. In 1966, Henry K. Beecher, anaesthesia professor at Harvard, included Willowbrook among twenty-two studies whose ethics he questioned, in an article on the ethics of clinical research.[63] Criticism of the experiments from an ethical standpoint continued over many years, and will be discussed in more detail shortly. It is important to note that many of Krugman's colleagues in the hepatitis world stood by him, organising the second international symposium on viral hepatitis in 1981 as a tribute to Krugman,[64] defending his experimental protocols and 'assurance of truly informed consent'.[65] The foreward to this volume ends with a quote from what must be the most execrable praise-poem ever penned:

> To this man, this friend, this Krugman, Saul

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[62] For results of Willowbrook studies, see (inter alia): S. Krugman, J. P. Giles and J. Hammond, 'Infectious hepatitis. Evidence for two distinctive clinical, epidemiological and immunological types of infection', Journal of the American Medical Association, 200 (1967), 365-73; for view that these studies 'represent an important contribution to our knowledge', see: 'Is serum hepatitis only a special type of infectious hepatitis?', Journal of the American Medical Association, 200 (1967), 407.

[63] H. K. Beecher, 'Ethics and clinical research', New England Journal of Medicine, 274 (1966), 1354-60; see also: H. K. Beecher, Experimentation in man (Springfield, Illinois: Charles C. Thomas, 1958)

[64] W. Szmuness, H. J. Alter and J. E. Maynard (eds), Viral Hepatitis: an International Symposium (Philadelphia: Franklin Institute Press, 1982)

[65] R. W. McCollum, 'Tribute to Saul Krugman, M.D.', in Szmuness et al, Viral hepatitis, p.xxii.

I convey the respect, and the pride,
and the thanks of us all.
When others might wither, this tree stands tall.
In the autumn of his life, his leaves will not fall.
This is the man whose life we're honoured to recall
This is the man we love, this Krugman, Saul.[66]

What ever else is lacking, the verse conveys an emotional solidarity between clinical researchers, suggesting that they all felt vulnerable to the attacks which had apparently made Krugman's life a misery for many years.

What had Krugman achieved with the Willowbrook experiments? Foremost was the distinction between two types of hepatitis which he labelled MSI and MSII, corresponding to A and B; the first having a faecal-oral route of transmission and a shorter incubation period and the second a mainly parenteral route of transmission and a longer incubation period. There was some suggestion that MSII was transmissable by mouth, but to a lesser degree. McKee, in an historical review in 1988, noting the previously accumulating evidence for two distinct types of viral hepatitis, states that: 'The existence of separate hepatitis A and B viruses was finally confirmed by Krugman' in the Willowbrook experiments.[67] McKee cites MacCallum's 1947 paper, but not the 1951 MRC report which covers the British wartime hepatitis studies in full detail.

Krugman himself, in a 1978 overview paper, cites another

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[66] Excerpt from 'Who is this man named Krugman, Saul?' by H. J. Alter (one of the editors), in Szmuness et al, Viral Hepatitis, 'Foreword' by the editors, p.xix.

[67] C. M. McKee, 'Hepatitis B in Northern Ireland - who should be immunised?', submission towards part 2 of MFCM exam, 1988, Chapter 3: Historical overview, p. 10.

MacCallum paper, together with five other human transmission studies from the 1940s, as precedents for his own work; he omits the 1951 MRC report.[68] His own interest, according to this account, was sparked by a symposium on laboratory work on hepatitis, sponsored by the National Academy of Sciences National Research Council and the Armed Forces Epidemiological Board, at New York University and Bellevue Hospital in 1954. The comprehensive failure to propagate hepatitis in laboratory animals pointed to the necessity for further human experiments. Krugman does not here mention that his subsequent research was partly funded by the United States Armed Forces; according to the historian William Muraskin, the Army was 'the major sponsor' of Krugman's Willowbrook work.[69]

In his 1978 account, among his summarised results, Krugman lists the observation:

> that HB could be spread from person to person following the type of prolonged, intimate contact that involved sharing of excretions. Thus, it was clear that a parenteral [e.g. inoculation] type of exposure was not the only mode of transmission of HB infection.'[70]

Although the group had published on the possibility of oral transmission of MSII, the singling out of 'intimate contact' here seems a post hoc recognition of an important facet whose significance really only became clear to clinicians during the 1970s, and was not originally picked up by Krugman: that is,

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[68] Krugman, 'Perspectives on viral hepatitis'.

[69] Muraskin, 'Silent epidemic', p. 282; see: S. Krugman and J. P. Giles, 'Viral hepatitis. New light on an old disease', Journal of the American Medical Association, 212 (1970), 1019-29, for acknowledgement of contract from the US Army Medical Research and Development Command among others.

[70] Krugman, 'Perspectives on viral hepatitis', p. 6.

sexual transmission.

The other outcome of the Willowbrook experiments - apart from the confirmation of two types of hepatitis - which is often quoted as a valuable breakthrough, was the preparation of a crude vaccine by boiling serum containing the hepatitis B virus. MacCallum had also attempted to inactivate the virus; he had not found a satisfactory means, though irradiation held some promise.[71] What MacCallum had not done was to administer infective serum to the same volunteers who received treated serum; in other words his interest was in rendering the serum used in blood transfusion safe, rather than finding a vaccine. In this sense, Krugman was definitely taking a step further than his predecessors. However, the later development of an active vaccine depended heavily on the recognition of the antigen by Blumberg;[72] Krugman's vaccine was too experimental to be tried outside Willowbrook, where it was only used on a small group of children.

There is another catch in the vaccine story at Willowbrook. Early in his investigations there, Krugman had managed to reduce hepatitis by some 80 per cent, by administering gamma globulin, an established 'passive vaccination' prophylaxis for hepatitis.[73] Krugman's work on the active vaccine is usually emphasized at the expense of the immunoglobulin findings. Yet

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[71] MacCallum, Infective hepatitis, p. 128.

[72] See Chapter 3, below.

[73] L. Goldman, 'The Willowbrook debate', World Medicine, 7 (1971), 22.

from the viewpoint of inmates and staff, his use of gamma globulin was more effective. Whilst his transmission experiments were continually justified on the grounds that most children admitted to Willowbrook were bound to catch hepatitis, Krugman's own work with passive vaccination showed this need not be the case.

A final aspect of the Willowbrook work should be considered as a partial explanation for the support for Krugman among his colleagues:

> Many thousands of serum specimens collected over a period of about 20 years have been stored in a "serum bank". These valuable sera were obtained before, during and for many months and years after onset of HA and HB [hepatitis A and B]. These pedigreed materials have been shared with many investigators who have been actively engaged in hepatitis research.[74]

The passage of clinical material between research laboratories can be interpreted - in a version of anthropological theories of gift exchange - as a means of incurring obligation, on the one hand, and securing a share of privileged access to knowledge, on the other. Almost certainly, such gifts help to cement bonds of loyalty whether between patron and client, or between equals.[75] Krugman at Willowbrook was mining a rich seam of hepatitis-infected blood from the mentally retarded children there;[76] parcelling out the serum for years to come probably helped him to survive in an increasingly hostile environment.

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[74] Krugman, 'Perspectives on viral hepatitis', p. 7.

[75] See: Stanton, 'Blood brotherhood'.

[76] Krugman and Giles, 'Viral hepatitis. New light', published in 1970, mentions 2,500 serum specimens from 700 'patients' [children].

Ethical issues in MacCallum's and Krugman's hepatitis investigations

Bynum, writing on the history of human experimentation,[77] draws a contrast between two books by medical men, books with similar titles but separated by over twenty years, with very different standpoints: Mellanby's Human guinea pigs of 1945,[78] and Pappworth's Human guinea pigs: experimentation on man of 1967.[79] Mellanby discussed without qualms his wartime researches into scabies, using conscientious objectors as subjects, taking the view that medical research was seen by the participants as a valid alternative to military service. Pappworth on the other hand presented a highly critical review of a whole range of clinical research on human beings; his book brought him hostility from fellow professionals but is a standard reference in subsequent medical ethics. The gap between these two, and the shadow of the postwar Nuremberg Trials, illuminates a pattern which we may trace as emerging again in the contrast between the British wartime hepatitis experiments and the American hepatitis experiments of 1956-71.

There is a problem in making this comparison. The debates are

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[77] W. Bynum, 'Reflections on the history of human experimentation', in S. F. Spicker, I. Alon et al (eds), The use of human beings in research with special reference to clinical trials (Dordrecht, Boston, London: Kluwer Academic Publishers, 1988), pp.29-46, esp. pp.29-30.

[78] K. Mellanby, Human guinea pigs (London: Victor Gollancz, 1945)

[79] M. H. Pappworth, Human guinea pigs: experimentation on man (Boston, Mass.: Beacon Press, 1968). This follows Beecher's 1958 book and 1966 article cited above, n. 63.

about Willowbrook, and MacCallum's work does not appear in the ethical literature. This presumably reflects the changing social context of medical research, which produced these ethical debates of the postwar period. It may not be historically valid to compare the ethical implications of the two sets of investigations, given that 'medical ethics' is not a timeless concept but one that has grown and changed. In any case, making such a comparison is difficult, since one set of investigations has been copiously covered in the literature, and the other not at all. Here, a brief discussion of the Willowbrook debate will be followed by an equally brief, very tentative, comment on MacCallum's experiments.

Following Beecher's 1966 article, the Journal of the American Medical Association continued to voice support for Krugman, alongside further Willowbrook papers - despite giving a favourable review of Beecher's work on medical ethics.[80] The debate over Willowbrook spilled over into the British journals which, like the American medical press, tended to be impressed by Krugman's work. In 1971, Stephen Goldby, a doctor at the Radcliffe Infirmary in Oxford, wrote to The Lancet asking if it could be right to perform an experiment on a child when no benefit could result to that individual; in his view, the answer must be 'no'.[81] Although The Lancet printed replies from Krugman himself and other doctors including Pasamanick of

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[80] Krugman, Giles and Hammond, 'Infectious hepatitis', and Editorial, 'Is serum hepatitis a special type?' (1967).

[81] S. Goldby, 'Experiments at the Willowbrook State School' (Corr.), Lancet, 1971 (i), 749; for comment on Krugman's studies of the sort Goldby objected to, see: 'Australia antigen and hepatitis' (Editorial), Lancet, 1971 (i), 487-8.

the New York Department of Mental Hygiene - involved in the Willowbrook project - its subsequent editorial policy was critical of the experiments.[82]

The justification for the Willowbrook experiments had been countered at several levels. The argument that children entering the institution were likely to be infected with hepatitis, and therefore would be no worse off with a controlled dose of infection, was challenged by Krugman's own success with immunoglobulin.[83] Parental consent could not, according to many commentators, justify experiments on children in any case, but especially when children were unable to comprehend anything of the proceedings. The successful outcome of the experiments was not a vindication either, since ethical validity must be present from the outset, and must be assessed independently of the scientific outcome. Above all, patients should not be used for experiments that might cause them harm, even if others might benefit.

Since the last argument is the strongest, most comprehensive one, demolishing any justification on grounds of outcome, it may seem superfluous to add that the Willowbrook experiments were anyway largely duplicating the MacCallum experiments. Nevertheless, the point is worth making, since it has escaped attention elsewhere. When MacCallum was asked why he thought Krugman underplayed the British work, he replied that

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[82] Ushered in by an editorial comment immediately following Goldby's letter; see subsequent correspondence in same issue.

[83] Goldman, 'Willowbrook debate', 21-2.

communications were poor during and after the war; although the articles in the medical journals were available, they told only part of the story, and it was very possible that Krugman had not actually read the full MRC report on hepatitis.[84] If that were so, it cannot be called unethical, but it was more than unfortunate. On the other hand, MacCallum's conclusions may really have seemed to leave much unexplained; perhaps only in retrospect does the important distinction between two types of hepatitis seem so clear.

Should the work of MacCallum and colleagues be seen as essentially different in ethical terms from that of Krugman? The absence of published comment has been remarked; scraps of opinion gathered from other researchers are contradictory and seem to depend on the informant's personal relations with MacCallum. Some say that such use of 'volunteers' was quite unethical, since no-one knew what would happen when they were inoculated with hepatitis. This echoes a 1951 comment by R. A. McCance, profesor of experimental medicine at Cambridge:

> The risk in any experiment depends very much on whether the investigator knows that he will always retain control of the situation. To inoculate somebody with icterogenic [jaundice-inducing] serum is a risk that I personally would never take, nor would I ever have cared to take it even before the risks were so well known, for once the inoculation had taken place I would have lost control.[85]

MacCallum believed that the low mortality in recipients of the hepatitis-contaminated yellow fever vaccine pointed to the probable containability of the infection; others would say he

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[84] F. O. MacCallum, personal communication, 19 May 1992.

[85] R. A. McCance, 'The practice of experimental medicine', Proceedings of the Royal Society of Medicine, 44 (1951), 189.

was simply very lucky not to have had fatalities among his experimental subjects.

Supporters of MacCallum would also point out that he first experimented on animals, exhaustively; that the volunteers for his human experiments were adults, and in the case of arthritics might benefit from the infection; and that the human experiments ceased the moment peace was declared. These were strictly wartime experiments, in which the primary justification for carrying out the work on human volunteers was the need of the military to understand and contain the problem of hepatitis. However, in the case of other nations, military requirements are not held to justify experiments that would otherwise be unacceptable. And if hepatitis infection was thought to aid arthritics, why not continue after the war? Perhaps the greatest difference between these and the Willowbrook experiments, in terms of ethical issues, lies in the age and mental condition of the 'volunteers'. However, the adult, mentally sound arthritis patients were not fully informed of the nature of the experiments - especially the source of the infective material - and the archival evidence cited here shows that the Ministry of Health and the chair of the MRC Jaundice Committee were acutely aware of the objections that might be raised. Their great uneasiness over this series of experiments probably explains why they ceased when the war ended and may well explain why publication of the full report was delayed. Did the chief difference in context between the wartime and postwar studies lie in the degree of secrecy, with increasing openness of debate in the postwar

period eventually capsizing Krugman's work?

Conclusions

This chapter outlined changing ideas about viral hepatitis through the first half of the twentieth century and suggested that developments in the concept of 'the virus' itself were important for further research. By mid-century, the notional 'infectious' and 'serum' types of viral hepatitis had been identified as following different routes of infection, the former through the mouth (faecal-oral), the latter via other routes (parenteral), and having different incubation periods (20-40 compared with 60-90 days). MacCallum, who led the British wartime research team which established these distinctions, coined the terms 'hepatitis A' and 'hepatitis B' for these two types. Awareness was also beginning to grow during the war of hepatitis in clinical settings, such as the blood transfusion service, which were to become important foci for concern over hepatitis B in the postwar period.

Means of transmission of hepatitis B other than via infected needles or infectious blood or serum were not known, but could be postulated. MacCallum regarded it as inherently unlikely that a virus could survive if it depended entirely on the technology of the needle; unless it was something new and rare, there must be other means of transmission. The notion that some people became passive carriers of the disease rather than exhibiting overt symptoms was also induced from these studies, but the extent of infection in the British or any

other population was a matter of conjecture.

A further, prolonged, series of hepatitis studies conducted at Willowbrook, a special school in New York, between 1956 and 1971 by Krugman and colleagues, produced similar results to those of the British wartime studies. Ethical issues raised by experiments using mentally retarded children at Willowbrook have been widely discussed elsewhere and were briefly reviewed in this chapter.[86] A range of justifications offered at the time and afterwards, including production of an experimental vaccine, were not seen as valid. A question was raised here, as to apparent failure to learn from earlier British studies.

The ethical debates, which have changed over time, leave another question: who wanted the research done, and why? Both the British and the American hepatitis studies were backed by their respective armed forces. Hepatitis was regarded as a hazard in the forces, especially in wartime, when crowding of troops in unhygienic conditions could result in outbreaks of hepatitis A, and mass inoculations could result in outbreaks of B. The other major area where hepatitis B was recognized as a problem was in the blood transfusion service. The point was raised in the Introduction, that policy needs may set the agenda for research, or allow previously unrecognized research to be seen as valid. During and after the war, the need to understand hepatitis B was growing, as the next chapter will indicate.

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[86] See also: S. E. Lederer, 'Orphans as guinea pigs: American children and medical experimenters, 1890-1930', in Cooter, Name of the child, pp. 96-123.

CHAPTER 3: POSTWAR DEVELOPMENTS AND THE AUSTRALIA ANTIGEN DISCOVERY [1948-1971]

The previous chapter showed how wartime conditions produced outbreaks of jaundice, prompting research which distinguished two main routes of infection. Epidemics of hepatitis A could be more readily contained once it was known that the putative virus was transmitted by faecal matter contaminating food or water. This variant will henceforward play little part in the present account, although it should be borne in mind that it remained difficult to distinguish clinically between types of hepatitis in cases of acute jaundice.

The transition from wartime to postwar conditions forms an important background to later research and policy on hepatitis B, in general and particular ways: the first part of this chapter will discuss in brief a number of changes in postwar medicine. While clinical research was developing and changing in many parts of the world, the new structures of the National Health Service in Britain[1] opened up greater possibilities for such research than had been available in this country before the war. Ways of handling hospital infection were affected by the new pattern of hospital organization. Special services, first established as wartime emergency services - blood transfusion and public health laboratories - expanded and consolidated their functions. Many new technologies were introduced or expanded, including mass inoculation and renal

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[1] These organizational structures varied between component countries of the UK, as pointed out in Harrison, Hunter and Pollitt, Dynamics of British health policy, pp. 2-3.

dialysis. All of these are relevant either to the spread of hepatitis B, or to its control: in some cases, to both spread and control. Other areas where hepatitis B spread, however, remained relatively 'invisible' during this period, although some doctors saw it as a disease of needle-using drug takers.

At the same time, various branches of research allied to virology were developing, though with little overt reference to hepatitis A or B. Hepatitis had proved difficult to transfer to animals and now proved equally difficult to grow in tissue cultures, an apparently essential tool of postwar virology. From biochemistry, via genetics and the study of blood proteins, came an inadvertent discovery that had direct bearing on hepatitis B. This was a previously unidentified antigen, which turned out to be an antigen of the hepatitis B virus: it took several years and the work of a number of co-workers before the connection was established, so unlikely did it initially appear. This antigen was referred to as the 'Australia antigen' (for reasons that will be explained), reflecting uncertainty over its identity. The middle sections of the chapter will outline the path by which the American researcher Baruch Blumberg made the initial finding; and responses in the UK, at the point when the significance of Australia antigen was open to debate. Then in the last sections, contributions made by two British researchers will be discussed in terms of the type of work involved, and networks of reciprocal interest, which are the focus of further discussion in Chapter 6. These steps in research on hepatitis B are linked with the structural changes discussed

earlier, especially developments in clinical research.

Postwar medicine

The new National Health Service established in 1948 was very hospital-centred, entrenching the power of hospital doctors and creating new openings for them. Among other effects, research - clinical research - was facilitated, as more hospitals were upgraded to teaching hospital status and bigger budgets were provided to enable departments of medicine, surgery and obstetrics and gynaecology to be run in a similar way to science departments.[2] The concept of medical departments with integrated teaching, research and practice components, after the American and German model, had been around since the early twentieth century. There had been attempts to implement it primarily with Rockefeller money, but a major problem had always been the discrepancy between the salaries and status of university professors and the much higher rewards available on the open market, in private practice allied with an honorary appointment as a consultant at a leading teaching hospital.

The advent of the NHS made it easier for doctors to devote less time to private practice and more time to research. They were provided with space and funds for research in hospitals which had relatively little money for capital building until

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[2] For important interwar initiatives including the work of T. R. Elliott and Thomas Lewis at University College London, and the expansion of clinical research in the immediate postwar period, see: Booth, 'Clinical research'.

the 1960s, and which invested instead in personnel. There was a move away from the municipal hospital pattern, with its medical superintendent; as in the old voluntary hospitals, most patients were brought under the control of consultants. As hospitals were upgraded, clinics and laboratories were added, to bring the often poorly-equipped ex-municipal hospitals up to regional standard. In addition to the greatly expanded opportunities provided by hospital restructuring, as Booth has pointed out, the MRC had more money available than ever before and was setting up more research units; and the university sector was expanding rapidly. Together these developments provided an unprecedented base for the 'exploitation of the new biological sciences in the study of human disease'.[3]

Although this chapter will focus on research, it is important to consider aspects of the postwar organization of medicine that will be relevant to other aspects of this history; in any case, they often have some research functions as well. The Public Health Laboratory Service was a continuation of the wartime emergency service, set up to counter germ warfare; its initial emphasis was therefore on bacteriology. Its expanding national network of laboratories was under MRC direction until 1960, when the Ministry of Health took over; its organisation was parallel to, but somewhat separate from, that of hospital laboratories, with an emphasis on preventive, epidemiological work.[4] During the period of MRC supervision:

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[3] Ibid, p. 233.

[4] Webster, Health services since the war, p. 317.

> the whole administration was on a purely personal basis, laboratory directors were able to approach the headquarters office directly and often solve problems or obtain urgent supplies with a speed that was the envy of those working in National Health Service laboratories who had to work through committees and often experienced long delays.[5]

It appears that even after the Ministry of Health took over, the PHLS retained its separate identity, although in some regions it merged into the hospital service more than in others. At both regional and central levels, it developed research functions to complement its reference and, later, surveillance work.[6] It was, above all, ideally placed to gather epidemiological evidence on a wide range of infectious diseases.

As mentioned above, under hospital reorganization of 1948, the role of medical superintendant was abolished with the result that no single person had similar responsibility for dealing with outbreaks of infectious diseases within hospitals. The function could be taken on by the consultant in charge of the nearest PHLS laboratory; or the chief bacteriologist in the hospital might be called upon to deal with the problem. But until the appointment of Control of Infection Officers in many hospitals, there was no formal system of co-ordinated response in case of outbreaks. It could be argued that a more relaxed attitude to hospital infections was developing because antibiotics increasingly seemed to promise a cure for every

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[5] R. E. O. Williams, Microbiology for the public health: the evolution of the Public Health Laboratory Service 1939-1980 (London: Public Health Laboratory Service, 1985), p. 36.

[6] Ibid, p. 161: the Communicable Diseases Surveillance Centre (CDSC) at the central PHLS was set up on the recommendation of the Cox Report after the 1973 smallpox incident at LSHTM.

ill. The pre-war spectre of an outbreak of streptococcal infection, affecting patients and staff indiscriminately, had been laid to rest with the mass production of penicillin. This may partly explain the very strong responses to outbreaks of hepatitis B in renal units in the 1960s, when modern medicine had nothing to offer to help the afflicted.

Renal dialysis could be seen as another child of the war. Experimental work had been done in the interwar period, but the first successful haemodialysis (that is, leading to recovery of the patient) took place in Holland in 1942.[7] Subsequently the technique was refined and further developed in Scandinavia, Britain and the US, and by the 1950s units had been established to provide dialysis for acute renal failure. Many individuals undergoing this treatment received copious blood transfusions, in addition to having their own blood removed and circulated around the dialysis machine. There was thus a chance that they would receive a blood-borne infection and that it might be passed on to those tending them. However, the risk was not very apparent, until the advent in 1960 of a further innovation, the arterio-venous shunt, which allowed a patient to be repeatedly connected to, and disconnected from, the dialysis machine: it allowed dialysis to be used longterm, to sustain individuals whose renal failure was irreversible. Some would say it created a new

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[7] This was the work of Kolff in Kampen; but see: H. Klinkman, 'Historical overview of renal failure therapy - a homage to Nils Alwall', Contributions to nephrology, 78 (1990), 1-23, esp. 8 for suggestion that the 17th patient treated by Kolff with a rotating drum dialyser, and the first to survive, would probably have recovered without dialysis.

condition of 'chronic renal failure' or 'end-stage renal disease', applied to patients who previously would have been seen as moribund.[8] The serious outbreaks of hepatitis that occurred in renal dialysis units from the mid-1960s, following this extension of the technique to chronic kidney failure patients, will be described in the next chapter.

Another area where hepatitis was long recognized as a hazard, already mentioned in the previous chapter, was in blood transfusion. Like the PHLS, the blood transfusion service was a special service allied to, but not an integral part of, the hospital service.[9] Blood transfusion, which had been a little used, experimental technology in the earlier twentieth century, became a massive life-saving innovation during the Second World War, when an emergency blood transfusion service was organized for military and civilian casualties. The wartime emergency service laid the foundations for a co-ordinated, nationwide, blood transfusion service, tied in with the regionally-organized hospital service.[10] Regional Blood Transfusion Centres (BTCs) collected blood and distributed it mainly within their region, although both whole blood and plasma could be redistributed to some extent. Freeze-dried plasma had been widely employed during the war as an alternative transfusion material: its lower bulk and longer shelf life gave logistic advantages over whole blood or

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[8] Thanks to Professor C. Normand of LSHTM for this insight into 'end-stage renal disease' as a technology-dependent diagnosis.

[9] Webster, Health services since the war, pp. 319-21.

[10] In England and Wales. The Scottish service was more centralized.

plasma, but it invariably originated from pooled donations, carrying a greater risk of infection - as we have seen, it had resulted in hepatitis outbreaks when used in yellow fever vaccine. In the postwar period, the central Blood Products Laboratory (BPL) at Elstree, outside London, received blood and plasma from BTCs, which it used to develop such blood products as general and specific immunoglobulins used in boosting the immune system and combatting certain infectious diseases.[11] Other fractions were developed for treatment of inherited clotting disorders, notably Factor VIII for the more common form of haemophilia.[12] The hepatitis hazard escalated enormously, as larger pools were needed for manufacture of concentrated blood products.

America to some extent set the pattern for the expansion of clinical research discussed above; an international culture of science was developing in this period. Having set the scene for an exploration of research on hepatitis B, with a focus on the UK, this chapter first follows the career of an American researcher: Baruch Blumberg, whose discovery of the antigen of hepatitis B in the 1960s, together with progress towards making a vaccine, earned him a Nobel Prize in 1976. Blumberg himself has often pointed out that he was not working on hepatitis when he happened upon the antigen. He is as a prime example of the postwar breed of medical researchers, with training in medicine and biochemistry, supplemented with

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[11] Immunoglobulins are fractions of plasma, containing antibodies.

[12] Factor VIII was used for treatment of Haemophilia A. and Factor IX for the rarer Haemophilia B.

genetics, virology and later - less usual for a medical scientist - anthropology. It may have been this sort of combination, supported by generous institutional funding and a network of clinical researchers, that made possible the steps leading to the 'discovery' and its elucidation. UK responses, and the role of two British researchers in illuminating the nature of Blumberg's findings will be discussed in the latter sections of this chapter.

The story of the discovery of Australia antigen has been told many times, and its implications for the understanding of hepatitis B are well known to scientists in this field.[13] Why, then, recount this episode here? The intention is not to repeat the well-worn trail but to offer fresh interpretations. While the scientific papers read as though the puzzle of hepatitis B was being purposefully unravelled, by Blumberg and successive investigators (for our purposes, notably Dane and Almeida), the oral record reveals that none of these people set out study hepatitis B. A leading figure in this country who tackled hepatitis B more directly - Zuckerman - was less successful in making a major breakthrough (see Ch.6 below). Looking further into the ways in which researchers are drawn into work in a particular field can offer insights into the interrelations between individual scientists and clinicians, research teams, and institutions.

Individual stories also help to pinpoint the role of ideas or

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[13] The antigen discovery was widely regarded as such an important turning point that, initially, it had been intended to take it as the starting date for this study.

technologies in enabling research to move in certain directions; blockages in other directions may be equally important. The clinical problems of hepatitis B often appear distant in these narratives, yet they are constantly present in the form of 'clinical material' - that is, patients, or samples of blood or serum - which play a crucial role in these developments, just as they did in the earlier hepatitis studies discussed in the previous chapter. It could be hypothesized that the outbreaks of hepatitis in renal units in the late 1960s, as well as providing an impetus for research and policy developments, actually assisted the recognition of the virus, by providing more active samples than were normally available. Further, it will be argued that transatlantic advances may have received a disproportionate amount of recognition, since the discovery of the virus itself and of the core particle both took place in the UK.

Blumberg and the discovery of Australia antigen

Blumberg was medically qualified (New York), when he came to Oxford in 1957 to do postgraduate work in the biochemistry department, on the properties of viscous compounds like synovial fluid and aqueous humour, under Sandy Oxton, the Reader in Physical Biochemistry. While carrying out his research, he became enthused - if not sidetracked - by discussions with Anthony Allison, a white Kenyan studying in the Zoology Department which had a strong population biology

strand.[14] E. B. Ford, a leading lepidopterist in the department, had developed a definition of 'polymorphisms' based on studies of variations in wing patterns of moths and butterflies. Blumberg and Allison speculated about applying the notion of polymorphism to human populations. From his student days, when he had spent an elective period in Surinam, Blumberg had been fascinated by variations in people's responses to a given disease, such as filariasis, depending on the population they originated from.[15] He and Allison discussed ways of looking at variations - polymorphisms - in serum proteins of various populations, which might help to explain variations in response to disease.

Around this time, they became aware of a new method of separating serum proteins: electrophoresis, developed by Oliver Smithies. This analytical technique, using starch gel gradients, has been described by Blumberg as the 'minor equivalent of a new microscope'.[16] Armed with this effective but simple new technology, Blumberg began a series of summer trips to areas of the world with clearly defined indigenous populations, combining the collection of blood samples with a public health function wherever possible. He has fantastic stories to tell of adventures among the Fulani of the Jos

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[14] Interview with B. S. Blumberg (Master of Balliol), 25 March 1992.

[15] Interview, Blumberg, 12 March 1991.

[16] B. S. Blumberg, 'The hepatitis B vaccine', talk given to Wellcome Trust Twentieth Century History of Medicine Group, Wellcome Institute for the History of Medicine, London, 9 Feb 1993.

plateau in northern Nigeria, or the Eskimos (Inuit) of Alaska.[17] When he returned to the States, to the National Institutes of Health (NIH) at Bethesda, he continued this pattern of summer trips collecting 'bloods', but augmented the range by asking others to send him samples too. Among these were sera from Australian aborigines sent by Dr Robert Kirk of the University of Western Australia, who 'had collected them as part of an extensive investigation of genetic traits in this interesting population'.[18]

Blumberg looked at reactions of multi-transfused patients in the US to antigens in samples from around the world. Multi-transfused patients could be seen as a potential catalogue of polymorphic variations: their blood might contain antibodies to a variety of antigens that occurred normally in only a small proportion of the local (US) population. Blumberg was joined at his NIH lab in 1960 by Tony Allison, who had also travelled in Africa collecting blood samples; at about the same time, a haematologist and technician joined the team. In 1963, they observed a reaction between the serum of a multi-transfused, haemophiliac patient from New York City, with serum from an Australian aborigine. They had no idea what this signified - Blumberg goes so far as to say that their investigations could not have been planned so as to find the cause of hepatitis, and that if they had been looking for it,

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[17] Blumberg, interview, 25 March 1992.

[18] B. S. Blumberg, 'A short history of Australia antigen', in W. Gerok and K. Sickinger (eds), Drugs and the Liver, 3rd international symposium, Freiburg, Oct 1973, (Stuttgart, New York: F. K. Schattauer Verlag, 1975), p. 9.

they would never have found it.[19]

Transferring in 1964 to the Fox Chase Institute for Cancer Research in Philadelphia, Blumberg continued to build his collection of samples of serum and plasma, but additionally had access to sample banks accumulated in the NIH and Institute for Cancer Research by other researchers. The new antigen, termed 'Australia antigen' after its aboriginal Australian source, was tested against a wide selection and found to be very rare in the normal US population, but more common in samples from Asia. Sam Visnich, the technician, when asked to select out multi-transfused sera, found the antigen was prevalent in leukemia patients.[20] The team then tested groups with a known higher than usual susceptibility to leukemia. One such group was Down's syndrome patients, and they were found to have a high frequency of Australia antigen - a 'gratifying' result because it fulfilled the prediction of an association with leukemia, and also allowed detailed study of subjects 'closer to home than the Australian aborigines' and other high frequency populations.[21]

After many findings which seemed to indicate that a person's Australia antigen status was fixed - being either positive or negative - there was great agitation when one of the Down's

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[19] Ibid, p.9. There was a previous finding which informed their next moves, involving a polymorphic low density lipoprotein system, but this seems important in retrospect mainly as demonstrating clearly to the team that they were onto something different.

[20] Ibid, p. 10.

[21] Blumberg, 'Australia antigen story', p. 8.

syndrome patients who had been negative on a previous test was found to be positive on a second test. The patient whose antigen status had converted was admitted to the Clinical Research Unit at Jeanes Hospital, attached to the Institute, and subjected to a wide range of tests. One of these was a liver function test, which revealed a form of anicteric (non-jaundiced) hepatitis, generating huge excitement among the investigators.[22] It now appeared that the Australia antigen was linked with hepatitis, an unexpected but clearly momentous finding, given the previous difficulty of investigating hepatitis.

Subsequent tests for links between the Australia antigen and hepatitis confirmed this finding. Sera from patients with a known history of chronic hepatitis, or from populations with a high incidence of hepatitis, were examined. Many of these studies were carried out in Africa and Asia, using reagents supplied by the NIH. They confirmed that in populations with a high rate of hepatitis, there was a greater prevalence of Australia antigen. Back in the US, the particles that constituted the Australia antigen were visualised using electron microscopy (EM); they were minute and lacked nuclear material, DNA, raising the question whether they represented a new form of virus, or an incomplete part of the virus.

By 1969, there seemed enough certainty that the Australia

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[22] A. I. Sutnick, W. T. London, et al, 'Anicteric hepatitis associated with Australia antigen: occurrence in patients with Down's syndrome', Journal of the American Medical Association, 205 (1968), 670-4.

antigen particles were identical with hepatitis B antigen for Blumberg and colleagues to propose using them, in a purified form, as a vaccine against hepatitis B. When this proposal was patented in 1971, its originators did not in fact know whether they had found the virus of hepatitis B, and could only postulate that a whole virus would have greater mass than the antigen particles and would thus be precipitated by centrifugation, leaving purified antigen, without infectious virus, to be used in the vaccine.[23] If the antigen had in fact proved to be the virus, as one hypothesis had proposed, there could have been trouble: but by this time, additional evidence was accumulating about the nature of the virus. The remainder of this chapter focuses on British responses and research immediately following the Australia antigen findings.

Australia antigen and hepatitis: UK views, 1969-71

When the observations of Blumberg and his colleagues were supplemented by others in the US and elsewhere, strongly supporting a theory that Australia antigen was associated with hepatitis, British investigators began to contribute to the debates. It is argued here that the role played by British researchers, especially in making components of the virus visible through electron microscopy, was crucial in solving important aspects of the Australia antigen/hepatitis puzzle. This puzzle had many elements, but perhaps the three that were most urgent at this stage can be summarized as follows: (i)

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[23] Blumberg, 'Australia antigen story', p. 10; Blumberg, 'Hepatitis B vaccine' talk.

The identity of the antigen - was it definitely the hepatitis antigen - and if so, which form of hepatitis? (ii) Was the Australia antigen itself the virus causing hepatitis B, or was it a non-viral particle? (iii) What was the explanation for the different immunological responses which led to some patients having an acute form of the disease, others having a chronic form, and yet others apparently having no reaction but becoming carriers?

By mid-1969, enough evidence was accumulating for the editors of The Lancet to feel it was worth publishing summaries of the current position - once in July and again in September. The July editorial mentioned, among other questions not yet resolved: 'Is the antigen in serum the virus particle itself, or is a viral protein, for example, also implicated?' and speculated on the common factor linking the oddly assorted groups of patients with persistent Australia antigen in their blood, perhaps due to 'an immunological defect'.[24] The origins of this discovery, embedded in genetic serological work, suggested that the antigen might have been an inherited trait, and this idea clearly still lingered.

The September editorial recalled the UK wartime hepatitis study, then ran through Krugman's investigation, 'a model of its kind', emphasising the findings on possible oral infection and on spread to 'contacts' - an aspect that was to become increasingly important. It used recent electron micrographs

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[24] 'Australia antigen and hepatitis' (Editorial), Lancet, 1969 (ii), 143.

to argue that Australia antigen was in fact the virus: 'Although the structure is not clear, these pictures are compatible with the idea that the antigen is a virus causing hepatitis'.[25] The identity of the antigen with serum rather than infectious hepatitis was emerging, but not yet fully established.

The journal also published current hepatitis research, including a report from a team at Yale on Australia antigen in acute and chronic liver disease,[26] and several articles on hepatitis in haemodialysis units, where outbreaks were beginning to be observed. In one of the latter, the authors used the term 'SH antigen' (serum hepatitis antigen) coined by Dr A. M. Prince of New York, and thanked him for 'the generous gift of his reference antiserum'.[27] At this time, there were few sources for the antigen and antibody, and one important role played by researchers like Prince and Blumberg was to disseminate these materials to other researchers. As the next Lancet example shows, recipients could then act as resource centres in their own locality.

Almeida and Waterson, whose further work will be discussed below, provided an important clarification of the 'carrier

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[25] 'Hepatitis virus' (Editorial), Lancet, 1969 (ii), 577-9.

[26] R. Wright, R. W. McCollum and G. Klatskin, 'Australia antigen in acute and chronic liver disease', Lancet, 1969 (ii), 117-121. (Wright was at the Radcliffe Infirmary, Oxford, when the article was submitted.)

[27] G. C. Turner and G. B. Bruce White, 'S. H. antigen in haemodialysis-associated hepatitis' (Liverpool), Lancet, 1969 (ii), 124. See also: 'Hepatitis virus and renal dialysis' (Editorial), Lancet, 1969 (ii), 989-90.

state', a notion which had been present in previous research in a blurred form, but which had chiefly derived from practical experience in the blood transfusion service.[28] Now Almeida and Waterson compared the sera of a symptom-free carrier, a patient with chronic hepatitis, and one who had died from acute hepatitis B. To compare the former, which had no antibody, with the other two, they added antibody produced in a rabbit. In their acknowledgements, they thanked Drs A. J. Zuckerman and P. E. Taylor of the London School of Hygiene and Tropical Medicine 'for doing the immunodiffusion tests and for making available to us the specific rabbit antiserum supplied to them by Dr Baruch S. Blumberg'.[29] The carrier had transmitted hepatitis 20 years previously, when his blood had been found to be responsible for three cases, one of them fatal. Samples had been saved and were now examined by electron microscopy, which revealed that the carrier had failed to form antibody to hepatitis B, thus remaining infectious, though himself apparently healthy.

Informants who played a role in hepatitis research in the UK tend, unsurprisingly, to emphasise the contribution of British researchers, and its relative neglect compared with US efforts

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[28] MacCallum and Krugman used material from patients with active hepatitis. Blumberg was initially finding hepatitis carriers without realising it; his subsequent recognition of the identity of hepatitis B depended on a patient acquiring the disease while under observation; see p. 98 above.

[29] J. D. Almeida and A. P. Waterson, 'Immune complexes in hepatitis', Lancet, 1969 (ii), 986. This paper, published in November, seems to represent work building on that reported in a paper accepted for another journal in June of the same year: J. D. Almeida, A. J. Zuckerman et al, 'Immune electron microscopy of the Australia-SH (serum hepatitis) antigen', Microbios, 2 (1969), 117-23.

- reminiscent of the trials which established the difference between hepatitis A and B, discussed in the previous chapter. Two notable contributions to be outlined below tend to support this view.

A rather different point emerges from a survey of the literature, combined with analysis of the career patterns of clinical scientists, their institutional affiliations and links with researchers elsewhere.[30] Progress in hepatitis research depended on a complex of factors, few of which were determined by the research programmes of funding bodies or institutions. Keeping abreast of the current literature was obviously important, but rather more important would appear to be command of techniques appropriate to a particular line of enquiry, which attracted fellow researchers and induced them to supply ideas and clinical material. The exchange of blood and serum leads to a notion of 'blood brotherhood' between investigators[31] - a sort of transatlantic tribal effort of altruistic scientists. However, international exchange in scientific endeavour can be a preface to bitter struggle, as the story of the France/US exchange between Montagnier and Gallo in AIDS research illustrates.[32] The apparent generosity

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[30] J. Stanton, 'Hepatitis research and career trajectories', talk given at Health Matters Symposium, Science Museum, London, 5 March 1993; there is less emphasis on careers and more on type and place of work in the published version, 'Blood brotherhood'.

[31] Stanton, 'Blood brotherhood'.

[32] Thanks to V. Berridge for pointing out this parallel. For an account of this rivalry, see: S. Connor and S. Kingman, The search for the virus. The scientific discovery of AIDS and the quest for a cure (Harmondsworth: Penguin, 1988, revised 1989)

of sharing should not mislead us: it may play a part in the battle for primacy. Sharing one's samples, for example serum containing Australia antigen, could establish indebtedness, of the recipient to the gift-giver;[33] it also ran the risk that the recipient might leap ahead in his or her research. This is, in a sense, what happened next with two of the British hepatitis B researchers.

David Dane and the virus of hepatitis B

David Dane is one of the unsung heroes of the hepatitis B story, if one wished to approach history in those terms. A clinician who trained as a virologist, he belonged to a slightly earlier generation than Blumberg. The background to his work on hepatitis was virological and clinical work on polio, in particular trials of polio vaccines in the 1950s, in Belfast, where Dane worked under Professor G. W. A. Dick. In Dane's own account, this experimental polio work was so nerve-racking that moving into another field seemed relatively attractive, despite the risks and difficulties of hepatitis research.[34] During the Belfast trials, Dick and Dane had administered live polio vaccine to their own and colleagues' children, fortunately without mishap; but they knew of at least one researcher who had committed suicide when an attenuated strain of virus had recovered virulence and given polio to recipients.

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[33] As expounded in: M. Mauss, The gift: forms and functions of exchange in archaic societies (London: Cohen & West, 1954) [Translation of Essai sur le don (Paris: P.U.F., 1925)]

[34] D. S. Dane, interview, 6 Aug 1992.

In 1965 Dane, now Reader in Microbiology at Queen's University Belfast, began a research programme aimed at identifiying the hepatitis viruses by electron microscopy, with the assistance of Moya Briggs. Since conventional tissue culture and animal methods of growing the virus had so far consistently failed with hepatitis, Dane looked for an alternative approach:

> I thought that EM negative staining techniques had developed to the stage where we could use them in much the same way as bacteriologists had used light microscopy to discover bacteria, like the leprosy bacillus, which they could not culture.[35]

Apparently, Dane and Briggs' EM technique was largely self-taught. As a first step, they learned to recognise a wide range of viruses from a variety of specimens - from patients, animals and tissue cultures - prepared with negative staining techniques. Dane was keen to develop an ability to read slides made from unpurified samples, in order later to be able to recognise what had not been seen before: the hepatitis virus.

During the following year, 1966, Dane and Briggs moved to the Middlesex Hospital Medical School in London with Professor Dick; a not uncommon instance of one appointment leading to the removal of a group or team to a new establishment. The hepatitis research lapsed for two or three years. Then in 1969, Dane was asked to test some of Professor J. W. Stewart's patients 'for the mysterious "Australia antigen"'.[36] One of the first was a haemophiliac patient, whose blood proved

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[35] D. S. Dane, 'Discovering the virus of hepatitis B', Transfusion Microbiology Newsletter, 11 (March 1991), 16.

[36] Ibid.

positive for Australia antigen when tested by Colin Cameron, Dane's colleague. Dane decided to take the further step of examining the sample under an electron microscope, utilising previously acquired expertise. Together with Cameron and Briggs, he saw round particles, larger than the small spherical or tubular antigen particles that had already been described many times. In a series of further samples from patients with hepatitis, they were able to repeat this sort of observation in two cases. Electron micrographs were produced to show the double-shelled larger particles juxtaposed with the smaller antigen particles. Publishing their findings in 1970, the team made several important suggestions: that the larger particle they had visualised was the infective virus of hepatitis B; that the outer coat of this particle was made of the same material as the Australia antigen particles; that the latter were excess coat material; that because these larger particles were denser they might contain nucleic acid.[37]

These findings were bound to cause something of a sensation in hepatitis research circles. There was considerable resistance, particularly in the US, before they became widely accepted.[38] The key article became a standard reference in subsequent papers on the structure of hepatitis B, and in some circles the viral body was referred to as 'the Dane particle'

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[37] D. S. Dane, C. H. Cameron and M. Briggs, 'Virus-like particles in serum of patients with Australia-antigen associated hepatitis', Lancet, 1970 (i), 695-8.

[38] J. Almeida, interview, 29 January 1993.

for many years.[39] In essence the visualization of the virus, together with the interpretations offered by Dane and his colleagues, cleared several questions hanging over the Australia antigen, showing the antigen previously visualized to be free excess surface antigen, identical with the surface antigen on the virus. Whereas the former was present in serum samples in enormous quantities, the virus was far scarcer, which explained why it had not previously been seen. The link with hepatitis B was confirmed by antigen-antibody testing using Australia antigen, as well as clinical observation.

As a result of this work, Dane was regarded as an expert on hepatitis B in the UK, asked to give evidence to the Rosenheim committee of 1970-72, appointed to serve on the Maycock committees in the 1970s, and on a hepatitis advisory group in the 1980s.[40] But while Blumberg gained international recognition, and was awarded the Nobel Prize for discovering the Australia antigen - and for further contributions in the field - Dane's achievements received more limited public reward, even within the UK. For example, Zuckerman, another hepatitis expert and clinician/virologist, became Professor of Virology at the London School of Hygiene and Tropical Medicine, and latterly Dean of Royal Free Hospital Medical School; Roger Williams, a liver expert also appointed to hepatitis commitees, heads the Institute of Liver Studies at King's College Hospital Medical School; but Dane did not gain

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[39] At Almeida's suggestion, according to one informant: J. Beale, interview, 26 Feb 1993.

[40] These committees are discussed in detail in later chapters.

a chair. The reasons for this are not clear but may be connected with the way Dane channelled his energies into local, rather than international networks. He continued to work at the Middlesex, liaising with the North London Blood Transfusion Centre and with the central Public Health Laboratory, playing a key role in the practical implementaton of policies on clearing the blood supply of hepatitis and preventing further outbreaks in renal units.[41] He also gave support to health workers, particularly doctors, facing the stigmatization of having been identified as carriers of heaptitis B.

Dane was definitely one of the key figures in UK hepatitis B policy formation and implementation, as well as having made a crucial contribution to the scientific understanding of the virus. The lack of recognition, in terms of public accolade and academic advance, is an interesting conundrum, only partially solved by the observation that he is an essentially modest man, perhaps lacking in ambition - facilitator of others' work rather than promoter of his own. Comparing his fortunes with those of Blumberg, the fact that the Australia antigen came before the Dane particle is probably less important than differences in the size and style of the citation 'market' either side of the Atlantic: Americans are more devout devotees of citations and cite publications by US authors more than overseas papers, on the whole.[42]

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[41] Further discussed in following chapters.

[42] See citation analysis in: Studer and Chubin, Cancer mission; the suggested UK/US contrast in hepatitis B citations is an untested hypothesis.

June Almeida and the core

Blumerg brought an antigenic soup to the notice of the scientific community; Dane focused in on the virus; June Almeida's contribution went farther into the structure of the virus, laying bare the core. Almeida's answer, when asked how she came to make a breakthrough in hepatitis B research, is that she happened to be in the right place at the right time.[43] By this she means, not once but repeatedly she was in a position to benefit from the expertise of those around her, to learn new EM techniques and to apply them in excellent laboratory surroundings. Finally, when she was somewhat of a recognised EM expert herself, she was in contact with the right people, who brought her material which yielded the secret that had eluded others (though it had been touched on by Dane and his colleagues). And although her EM work was morphological, structural and visual, with no first-hand clinical dimension, Almeida gained greater recognition than Dane for her contribution, probably because her convincingly clear pictures of the viral core enabled others to start unravelling the genetic material to be found there. Finally, the fact that she was a woman, not medically qualified, who had worked her way up from laboratory technician to scientist, made her perhaps less threatening in what was becoming a fiercely competitive sub-culture. Not that she was a shy retiring flower - Almeida was certainly a forceful personality who expected due respect. But she seems to have succeeded in winning co-operation from a wider range of co-workers than

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[43] Almeida, interview.

most in this field.

Almeida was trained in electron microscopy in a Toronto laboratory in 1958, when the technique of negative staining had just been introduced; she was fortunate to be in Toronto which was a leading virological centre.[44] Negative staining transformed the picture, allowing tiny virus bodies which had not been seen before to be visualised with sufficient clarity to enable Almeida to launch on a long process of classifying them according to shape. The technique also had diagnostic potential as she later explained:

> On the one hand, the technique of negative staining allowed direct studies of virus construction at a molecular level to be undertaken, and on the other hand, it allowed the electron microscope to become one of the fastest and most efficient means of identifying a virus.[45]

Almeida was clearly very good at using the technique. The way that she had developed it attracted the attention of Tony Waterson, a British virologist visiting Canada, and he invited Almeida to join him at St Thomas's Hospital Medical School in London. She was there from 1964 to 1967, then accompanied Waterson when he moved to the Hammersmith Postgraduate Medical School, where she stayed until 1972. Along the way, Almeida produced sufficient scientific papers, of sufficient merit, to be awarded the DSc for publications in 1970.

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[44] Almeida, interview. She mentions work carried out with A. F. Howatson and D. F. Parsons at the Ontario Cancer Institute in: J. Almeida, 'A classification of virus particles based on morpholgy', Canadian Medical Association Journal, 89 (1963), 787-98.

[45] J. Almeida, 'Practical electron microscopy', Lab-Lore (Wellcome Service in Laboratory Technology), 5,7 (April 1973), 252.

Almeida describes the next important step as also occurring through personal contact, when an American visitor introduced her to the idea of immune electroscopy. In this technique, antibody was added to a serum sample, causing antigen and virus particles to clump together, so that the antibody could actually be seen. Thus, smaller particles were made visible than previously thought possible - rather like negative staining in relation to viruses - for antibodies are far tinier even than antigens, being conglomerates of molecules. Immune electroscopy was an invaluable tool in Almeida's hands, allowing closer studies of the antigenic complexes of many viruses.

Following Dane's discovery of the virus of hepatitis B, Zuckerman, with whom Almeida already had links, appeared at her laboratory in the Hammersmith one day to ask if she would like to look at a sample of hepatitis B material. Almeida, along with Waterson and others, had already subjected the Australia antigen to electron microscopic scrutiny;[46] this time she was looking for, and at, the Dane particle. The help of two virologists from Northwick Park Clinical Research Centre was enlisted; according to Almeida their greatest contribution was to confirm that the virus could not be grown in tissue culture, an enormous drawback in terms of conventional virology but a vindication of the contribution of electron microscopy.[47]

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[46] Almeida and Waterson, 'Immune complexes in hepatitis'.

[47] Almeida, interview.

Almeida knew that the outer coat of the virus could be split to release an inner particle; Dane's original article shows an example of this phenomenon. However Dane did not secure adequately detailed pictures of the core to suggest more than the possiblity of a polyhedral structure. Almeida had greater experience with EM morphological studies of viruses. She stripped the lipid (fatty) coat with a detergent, and obtained core particles in good concentration, with the help of her Northwick Park colleagues. It was clear to her that the core particle conformed to the sort of structure expected of a virus - unlike the antigen particles she had previously examined. Moreover she could identify the morphology of the core (an icosahedron), and demonstrate that the sides were made of identical repeating units, with a given periodicity. It was possible to postulate that this was the body which entered the host cell, inserting its own nuclear material to instigate mass production of viral and antigenic material. The core discovery was published in 1971.[48]

About the time of this publication, Almeida was invited to a closed meeting in the US, called to discuss the state of knowledge about hepatitis particles. Despite initial scepticism from some participants, who were inclined to cling to the theory that the Australia antigen was a strangely deviant virus, Almeida was able to convince the assembled experts - through her micrographs of the core - that the Dane particle was the virus causing hepatitis B. The meeting

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[48] J. D. Almeida, D. Rubenstein and E. J. Stott, 'New antigen-antibody system in Australia-antigen-positive hepatitis', Lancet, 1971 (ii), 1225-7.

agreed upon standardised terminology for the particles that had so far been identified: the surface antigen was to be referred to as HBsAg, the core antigen as HBcAg, and the whole viral particle, the Dane particle or hepatitis B virus. However, it was some years before the term HBsAg came to replace 'Australia antigen' universally.

Conclusions

The first part of this chapter outlined developments on both the service and research side of the health service in the UK, in the two decades after the establishment of the NHS. These include specific sectors such as the blood transfusion service and Public Health Laboratory Service, which grew out of wartime emergency services, and general questions of changing notions about hospital infections, and changes in the organization of clinical research in the postwar period. Hepatitis B was partly seen, at this time, as associated with medical innovations such as blood transfusion, where it was recognized as the major hazard. Another medical innovation, renal dialysis, was about to gain a notorious association with hepatitis B, to be discussed in the next chapter. Yet in clinical laboratories where samples of blood and serum were routinely handled, it appears that blood was regarded as a non-hazardous substance.

The remainder of the chapter examined scientific research which has often been described as leading to 'breakthrough' in dealing with the problem of hepatitis B. Historical accounts

by scientists or doctors often use a progressive model (an extreme form of Whig history?), in which scientific advances lead to progress in medicine, especially the ability of scientific medicine to tackle disease. Within these sorts of histories, the role of the 'discoverer' is paramount: there may be a search for particular qualities of character that led that researcher to make that discovery. Yet each of the accounts given by three key players in work on the hepatitis B antigen and virus[49] shows a strong consciousness of the role of contingency, and the input of other workers. The role of chance or opportunity has long been recognised in scientific research, where it has been discussed under the charming term 'serendipity'. In framing a historical account, we seek to explain what surrounding events and changes enabled such apparently chance events to occur when they did.

A common element, stressed in the first-person interpretations recorded for this chapter, was a technical innovation or new idea: for Blumberg, the idea of polymorphism and the technique of electrophoresis; for Dane and Almeida, the technique of negative staining in EM; and for Almeida, the technique of immune electroscopy, also within EM. Such advances in technique can be seen as necessary but not sufficient pre-conditions for the findings on hepatitis B made by these researchers. Less tangible factors - location of research, and the researcher's position within research networks - emerge as important elements, overlapping with notions of

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[49] These three were not, of course, the only leading contributors: no slight is intended on other researchers by choosing to focus on Blumberg, Dane and Almeida.

'insiders' and 'outsiders' in research and policy. For hepatitis B, the exchange of ideas, techniques and samples of clinical material seems to have been crucial to the (informal) organization of successful research.[50]

The next chapter will look at events which coincided with the research discussed in this chapter: the outbreaks of hepatitis B in renal units, and policy-making on hepatitis B in these units, around 1970. The timeliness of the scientific contributions introduced in this chapter raises the question of whether it was purely a matter of coincidence. Perhaps the renal unit problem was in a sense part of the solution, by focussing the scientific gaze at the same time as providing plentiful samples of blood from patients at various stages of the disease.

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[50] These ideas will be further explored in Chapter 6.

CHAPTER 4: HEPATITIS B IN RENAL UNITS [c.1965-1972]

During the war, as recounted in Chapter 2, evidence of serum hepatitis as a side-effect of blood transfusion was gradually growing. With post-war extension of the blood transfusion service, hepatitis became recognized as the major hazard of blood transfusion, although it affected under one per cent of transfused patients in Britain.[1] This was clearly a matter of concern in all hospitals, and for any branch of health care involving blood transfusion. A more specific and concentrated series of outbreaks of hepatitis in renal dialysis units, in all countries which adopted renal haemodialysis for chronic kidney disease, shocked the medical community. Outbreaks started in 1965 in this country; their impact will be outlined in this chapter, while the following chapter will look at the blood supply. In 1970, the Department of Health set up two advisory committees: Rosenheim on the renal unit outbreaks and Maycock on hepatitis in the blood supply. Both reported in 1972; both recommended utilization of the newly available Australia antigen test, as part of the means of clearing their respective target areas of the hepatitis B hazard.

Following on from the second half of the previous chapter, on the discovery of the antigen which was a marker for hepatitis B infection, these chapters may, at first glance, appear to be presenting a triumphalist account of the application of a

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[1] P. L. Mollison, Blood transfusion in clinical medicine (Oxford: Blackwell Scientific Publications, 5th edition 1972), p. 603, mentions hepatitis B as the main serious consequence of receiving blood.

scientific breakthrough to solve the major problems associated with hepatitis B in the health care arena. It is not intended that the account should be read that way. Once the utility of the Australia antigen test was accepted, perhaps it was to be expected that it would be used to exclude hepatitis B from renal units and the blood supply; conversely, concern in these areas may have hastened acceptance of the test. The crisis in renal units began before the identity of the Australia antigen was known; the early UK response was shaped by local factors which subsequently facilitated use of the test. Other countries did not take up testing as a solution to renal unit outbreaks in the same way. And, as the next chapter will show, use of the test was by no means the end of the story for hepatitis in the blood supply, since blood products such as Factor VIII continued to be infected.

Further, the antigen test is not here presented as 'the solution' to 'the problem' of hepatitis B, because the predominant policy construction at this time focussed on areas of concern within the health arena, but virtually ignored hazards which affected far greater numbers of people - intravenous drug users, and gay men - even though these were beginning to be recognized. This sidelining of groups outside the health service continued through the 1970s and into the 1980s, and was only slowly overturned by the impact of AIDS on policy approaches. Thus the changing construction of a disease (hepatitis B) affected the way in which the usefulness of a new technology (the antigen test) was filtered.

The present chapter outlines the story of renal unit outbreaks of hepatitis B in the UK and of their resolution following the Rosenheim Committee of 1970-72. Important elements in clearing hepatitis B from renal units predate Rosenheim: work undertaken by individuals at the central PHLS; also, patterns of coping evolved at local level in renal units and associated public health laboratories. The way that these elements worked depended both on individual initiative and on the national network of public health laboratories - a particular feature of the UK - which partly explains the difference in approach here, compared with other European countries. Thus the antigen test was employed in a specific set of structural circumstances, which are often omitted from scientific accounts.

Renal unit outbreaks: local reports and PHLS 1968 guidance

The first kidney haemodialysis unit in the UK had been set up at Leeds in 1956, and wider application of this technology followed the introduction in 1960 of the arterio-venous shunt, which enabled repeated dialysis of patients with chronic kidney disease. By 1967, about 30 dialysis units had been established; these were usually fitted into existing hospital accommodation, but some were purpose-built, like the Liverpool unit set up in 1958 in a prefabricated block. With the extension of dialysis to chronic kidney disease, the number of patients treated exceeded the number of beds, since each patient attended for a session of dialysis two or three times a week. Despite meticulous attention to hygiene,

opportunities were created for the spread of infection, by the constant turnover of patients and sharing of dialysis machines.

There were other problems of infection: for example, in a few patients, streptococcal infection developed in the area where the arterio-venous shunt was inserted. But hepatitis was the greatest problem, not least because there was no cure, and initially, no means of determining which type of hepatitis was involved. In a series of widely dispersed outbreaks, each of which was lengthy, messy and frightening, both patients and staff were affected; although the total number of deaths was small, the cumulative effect was deeply shocking. Between 1965 and 1971, hepatitis was reported in ten kidney dialysis units, covering a wide geographical spread: Manchester, Liverpool, Charing Cross (London), Birmingham, Royal Victoria in Newcastle, Royal Free (London), Hammersmith (London), Edinburgh, Guy's (London), and Cardiff. There was a total of 357 cases with 18 deaths. Cases divided up into 206 patients, 122 staff and 29 contacts; twelve patients and six staff died.[2]

The first hepatitis outbreak began in the Manchester Royal Infirmary in the spring of 1965, when a surgical registrar, a male nurse and a female staff nurse fell ill with severe hepatitis; the staff nurse died. Several unrelated cases of hepatitis were being treated in the Infirmary, but these three staff cases seemed to be linked via their attendance on a

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[2] Rosenheim Report, p. 13.

patient with acute renal failure admitted for haemodialysis. This patient later developed jaundice. Two laboratory technicians who had handled samples from that patient also caught hepatitis. Two more patients coming in from other hospitals to the dialysis unit were infected; a house physician and a staff nurse fell ill following contact with these patients. There was a further death in this group.[3] The newspapers reported the death from hepatitis of a hospital porter on his honeymoon, although the hospital denied he had been in contact with the dialysis unit. Precautions against cross-infection, especially contamination with blood and faeces from patients, were stepped up. Staff considered to be at risk were offered immunoglobulin. More cases followed, though it was thought that immunoglobulin modified the course of the illness, at least in the case of one doctor. By 1966, five patients and eleven staff had suffered acute hepatitis, and there had been three deaths.

Three important points about the response to this first renal unit outbreak, expressed in a Lancet article summarising the events,[4] are worth noting. (1) There was no certainty which type of hepatitis was implicated: the term 'infectious hepatitis' was used in this brief Lancet notice, and both blood (for serum hepatitis) and faeces (for infectious hepatitis) were suspect. (2) There was a call for infectious

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[3] 'Hepatitis and the artificial kidney' (Annotations), Lancet, 1965 (ii), 1000, suggests this was a patient (i.e. on haemodialysis) but the Rosenheim Report lists three staff deaths and no patient deaths in the Manchester outbreak.

[4] Ibid.

hepatitis to be made a notifiable disease, so that more could be learned about the epidemiology of the forms that were presumed to be viral. (3) There was also a call for the use of the artificial kidney to be continued, especially in the treatment of acute kidney failure where a 'revolution' had been achieved. Thus despite the fatalities among healthy staff, and despite the continuing uncertainty around the etiology of the disease(s) involved, the risk of hepatitis outbreaks was not regarded by the public face of medical opinion as outweighing the advances in treatment offered by the artificial kidney.

In the next renal unit hepatitis outbreak, in Liverpool in 1967, there were no deaths, but the experience was clearly harrowing for all concerned.[5] Staff who suffered hepatitis refused to work again in the renal unit. Moreover, during the outbreak which lasted for nearly a year, there were staff shortages as hundreds of person hours of work were lost through illness. Liverpool saw the problem in terms of a hazard to staff who contracted hepatitis from the blood of patients, who had probably received the virus in blood transfusions given as part of the dialysis treatment.[6]

At Charing Cross there was also an outbreak in 1967, with 15 patients but no staff infected. Here, the problem was

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[5] The total number of cases in the Liverpool outbreak between 1966 and 1971 was 55, with 15 patients, 7 contacts and 33 staff affected: Rosenheim Report, p.13; it is unclear how many were ill during the initial phase lasting about a year.

[6] P. O. Jones, H. J. Goldsmith, et al, 'Viral hepatitis: a staff hazard in dialysis units', Lancet, 1967 (i), 835-40.

interpreted locally as one of patients at risk from a hospital infection.[7] Charing Cross used immunoglobulin to protect staff and patients, on the assumption that they were dealing with infectious hepatitis (hepatitis A). A difference in approach between two units, based on different experiences of the disease, became a focus of debate.

As consternation grew at local level, it was reflected among the growing fraternity of dialysis experts, some of whom had been meeting at intervals in an informal group at the Department of Health and Social Security. In 1967, Hugh de Wardener of Charing Cross, who was chairing this DHSS dialysis group, called on the PHLS headquarters at Colindale to clarify the issue of immunoglobulin as a protective agent for those exposed to risk of hepatitis infection. Both Charing Cross and Liverpool had used immunoglobulin supplied by the PHLS: Charing Cross considered it to be effective, while Liverpool claimed it was virtually useless. The Director of the Epidemiological Research Laboratory at PHLS, Dr M. T. Pollock, asked Dr Sheila Polakoff to attend the dialysis group meeting.[8] Polakoff wished to settle the dispute by randomly allocating those at risk to one of two groups, to receive immunoglobulin or not, but she found that opinions were too strongly divided to allow this sort of trial to go ahead.[9]

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[7] In a second phase in 1968-71, 64 patients but only one staff member were affected: Rosenheim Report, p.13.

[8] Polakoff was working on measles, in the communicable diseases section of the PHLS headquarters at this time: S. Polakoff, interview, 14 October 1992.

[9] Polakoff, interview.

Instead, the upshot of the meeting was that 20 of the renal units agreed to send in records of cases of hepatitis including results of liver function tests, so that the PHLS could monitor what was happening country-wide, looking at inapparent as well as apparent infection.

Through the next twelve months, Polakoff recalled, 'nothing much happened' except that Charing Cross, continuing to find patients with raised liver function (which indicated that they might be hepatitis carriers) was 'consuming gallons of immunoglobulin'.[10] Meanwhile, the PHLS set up a working party on dialysis units, which compiled an overview paper, outlining the major microbiological hazards of dialysis, and pointing to preventive measures that all renal units could be taking.[11] Hepatitis was aligned with shunt sepsis and issues around the hygiene of the dialysis equipment, although these - unlike hepatitis - affected patient health alone. The PHLS noted that one means of preventing the spread of hepatitis, the use of immunoglobulin, was recognised as problematic, with expert opinion still divided over its efficacy.[12] Patients' exposure to hepatitis could be reduced, by reducing blood

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[10] Ibid.

[11] Public Health Laboratory Service (Working Party on Haemodialysis Units), 'Infection risks of haemodialysis - some preventive aspects', British Medical Journal, 1968 (3), 454-60.

[12] A PHLS study of the efficacy of British immunoglobulin was published alongside the report on infection in renal units; this was aimed at control of infectious hepatitis in schools and other institutions, rather than renal units. See: 'Assessment of British gammaglobulin in preventing infectious hepatitis: a report to the director of the Public Health Laboratory Service', British Medical Journal, 1968 (3), 451-54.

transfusions (initially large and frequent); trying to provide each patient with their own machine; separating chronic from acute patients; using sterile disposable syringes. Overall management and hygiene of the units could be geared towards greater infection control. Above all, the PHLS placed responsibility for each site onto the hospital bacteriologist. Local decisions and procedures were emphasized repeatedly, accommodating a de facto devolution of control to regional, district and hospital level. Meanwhile, in 1968, notification of hepatitis was introduced, but it was not considered practicable to demand separate notification of A and B.[13]

There were two notable developments in 1969: the advent of the antigen test for serum hepatitis; and a further series of outbreaks of hepatitis in renal units, perhaps demonstrating the ineffectiveness of the 1968 PHLS guidelines. These hepatitis outbreaks varied in scale and outcome, with the largest at Guy's Hospital in London involving 89 patients, staff and contacts between 1969 and 1971, with no deaths, while at another London hospital, the Hammersmith, there were only seven cases but three deaths.[14] All dialysis units, whether or not they were directly involved, became haunted by

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[13] At this date, doctors had to rely on clinical signs (not very different for the two diseases); it is not clear to me why separate notification was not introduced after the antigen test for hepatitis B became available. Polakoff of the PHLS used laboratory reports on hepatitis B cases for her epidemiological work through the 1970s.

[14] As with the initial outbreak at Manchester, hepatitis deaths outside the unit could be recognized as associated with it, if there was a link; one such death at Newcastle's Royal Victoria Hospital where there were five cases of hepatitis in the dialysis unit was included in the total.

the spectre of hepatitis. The most terrifying scenario was played out at the Western General Infirmary in Edinburgh, where among 28 dialysis-associated hepatitis cases between 1969 and 1971, four members of staff and seven patients died.

While these outbreaks raged, the new tool of the antigen test was being applied to the problem. As early as July 1969, a report on the antigen status of cases in the Liverpool outbreak was produced by two workers at the Liverpool Public Health Laboratory.[15] They had aquired the reference antiserum for their tests directly from Prince, whom they thanked for the 'generous gift'. Their findings supported the 'hypothesis that a positive test for S.H. antigen is associated with the presence in the blood of the causal agent of serum-hepatitis'. Besides this finding, confirming that the outbreak involved serum rather than infectious hepatitis, they reported that the antigen could only be detected in the blood of staff members for the first two weeks after the onset of disease, while in the blood of dialysis patients it persisted with no diminution over time. Thus staff exhibited a stronger reaction to the infection, becoming more acutely ill but then eliminating the virus; patients with the antigen showed less acute hepatitis, or lacked overt symptoms entirely, but tended to become chronic carriers.

A further extension to these observations on the different course of hepatitis infection in staff and patients was

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[15] Turner and Bruce White, 'S. H. antigen in haemodialysis-associated hepatitis'.

provided by a team at the Royal Free Hospital in London.[16] There, they found that five patients with no symptoms of hepatitis retained antigen in their blood for a prolonged period, whereas three other patients who suffered clinical hepatitis subsequently became antigen negative. These three patients were regarded as fit before they were exposed to hepatitis infection, having been restored to health by dialysis, but the patients who became carriers were either still unwell or had been readmitted because of illness. Thus it appeared:

> ... that the two patterns of disease previously noted in staff and patients depend not on category but on the state of health of the subject when exposed to the virus. It appears that a person who is unfit at the time of contact with the virus may, for reasons as yet unexplained, be incapable of mounting the host/virus response (clinical hepatitis), thus retaining the antigen. It is our experience that when a state of physical health is achieved subsequently by adequate haemodialysis the carrier state nevertheless persists.[17]

The authors suggested screening for the hepatitis associated antigen to avoid introducing positive cases into renal units; at Royal Free they believed the test had enabled them to curtail what might have become a much more severe outbreak.

Local and central responses: the Rosenheim committee

Reading the accounts from various dialysis units in the medical press, and looking at events from the viewpoint of the PHLS (and DHSS so far as their viewpoint is discernible), we

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[16] A. H. Knight, R. A. Fox, et al, 'Hepatitis-associated antigen and antibody in haemodialysis patients and staff', British Medical Journal, 1970 (3), 603-6.

[17] Ibid, 605-6.

are confronted with two rather different versions of the resolution of hepatitis outbreaks. Essentially the same measures appear in both versions, but - unsurprisingly - there is an emphasis on local intiatives in the former, and on central efforts in the latter account. Thus the Royal Free article, just discussed, mentions the 1968 PHLS guidelines but regards screening and exclusion of hepatitis carriers, combined with ever-increasing use of home dialysis, as the solution in their case which can be transferred to other settings.

Similarly the Liverpool team, in an update on the outbreak at Sefton General which had caused 55 cases by 1971, note that enhancing their own original hygiene precautions with those recommended by the PHLS had failed to prevent futher cases.[18] Antigen testing revealed that inapparent cases were entering a new supposedly hepatitis-free unit established after the early phase of the outbreak. This group suggested complete segregation of three categories of patients: infected, non-infected and potentially infected. Immune staff - those who had recovered from an attack of hepatitis - should if possible be induced to return to work on the unit. In general, staff should be offered incentives to undertake this hazardous work.

Meanwhile Polakoff's PHLS study, of 21 dialysis units which had agreed to send regular reports, provided a more panoramic vision of the pattern of infection, enormously enhanced by the

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[18] B. J. Hawe, H. J. Goldsmith and P. O. Jones, 'Dialysis-associated hepatitis: prevention and control', British Medical Journal, 1971 (1), 541.

introduction of antigen testing. At this stage (1969), Polakoff recruited Yvonne Cossart of the Virology Reference Laboratory at Colindale,. who had been on the panel for the survey, to supervise antigen testing at PHLS headquarters for the participating units. A further seven units agreed to send blood samples, bringing the total to 28.[19] A new phase of the study, based on the antigen test, began in January 1970. Sera from all units were tested; thereafter sera from patients were tested at intervals of three months, and newcomers were tested on arrival. Where a new outbreak occurred, sera were tested more frequently. Liaising with consultants in charge of dialysis units, marshalling and analysing the data, were enormous tasks; persistance of hepatitis in some units undoubtedly amplified the pressure under which the two women worked. According to Polakoff, although the director of the PHLS agreed to her undertaking this antigen survey, no extra money, staff or premises were allocated; she and Cossart worked flat out with assistance from a medical statistician and presumably some laboratory support, but little else, from 1970 to 1975.[20]

By 1970, however, there were moves afoot at departmental level: in view of the serious nature of the outbreaks of hepatitis in renal units, the DHSS set up a committee to review the situation and recommend steps to deal with it.

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[19] Edinburgh was not included in the survey whereas three Glasgow units were.

[20] Polakoff, interview; another informant described Polakoff becoming ever thinner while Cossart gained pounds, as they reacted in opposite ways to the enormous pressure of work: E. Vandervelde, interview, 1 April 1992.

Without seeing the papers of the Rosenheim Commitee, as it came to be known (from the name of its chairman, Lord Rosenheim, an eminent nephrologist and consultant physician at University College Hospital, London), it is of course impossible to do more than speculate about the negotiations leading to the formation of the committee, or the nature of the evidence which it heard.[21] It was clearly framed as an advisory group to make recommendations on the hepatitis problem in renal units, rather than a commission of enquiry which might have sought to allocate blame. The situation was interpreted as a hazard and a misfortune, not anyone's fault.

Sir James Howie, head of the central PHLS at Colindale, and Dr (later Sir) William Maycock, head of the Blood Products Laboratory at Elstree, sat on the committee; there were also representatives from five of the hospitals whose dialysis units had experienced hepatitis outbreaks. These were consultant surgeons and physicians plus one chief technician. A professor of bacteriology from Dundee, a consultant physician from Glasgow, a nursing sister from Lambeth and a matron from Bristol were presumably called upon for the views of those involved in the issues of hepatitis prevention, without having experienced an outbreak. Dr C. E. Gordon Smith, Dean of the London School of Hygiene and Tropical Medicine, and Fellow of the Royal College of Pathologists,

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[21] My requests for clearance to look at these, and other papers relevant to hepatitis falling within the 30-year period, started with the Departments of Health and Social Security Departmental Records Management at Nelson in Lancashire and continued as far as Dr K. Calman, Chief Medical Officer, to no avail: corr. Aug-Oct 1992.

perhaps provided an overview,[22] while Dr Roger Williams, Director of the Liver Research Unit at King's College Hospital and Medical School could offer specialist insight into the impact of hepatitis on the liver.

Between October 1970 when it was appointed, and May 1972 when it produced a report, the group held thirteen meetings, taking oral and written evidence from clinicians and nurses in dialysis and transplantation units, and from microbiologists and epidemiologists. Comparative statistical data were obtained from the European Dialysis and Transplantation Association. There is no mention of technicians giving evidence although they figured prominently among the victims of hepatitis. Perhaps their views were thought to be sufficiently represented by the chief technician from Newcastle, Mr P. J. Dewar, who sat on the committee, and by Howie and Gordon Smith, the two pathologists. Certainly, Howie later appears as somewhat of a hero to technicians, despite the general hierarchical divisions between officers and ranks in clinical laboratory work.

Roger Williams remembered the meetings as being efficiently conducted, without a sense of panic because although the outbreaks were worrying, the numbers were small; there was some 'emotional attachment' when young doctors and nurses died, but he did not recollect the committee meetings actually

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[22] And an echo of the wartime MRC Jaundice Committee meetings which were held at LSHTM.

becoming emotional.[23] Level-headed common sense was the keynote of the group's report which stressed that anxiety over the hepatitis outbreaks must not lead to a defeatist attitude - by which, it may be assumed, the authors meant the closure of renal dialysis and transplantation units. Reassuringly, they claimed that: 'The problem is no different in kind from problems of infectious disease which have been met and overcome in the past'.[24] Previous situations where serum hepatitis had emerged as a problem were not called into play in the report, which rather implied that these hepatitis outbreaks were similar to the broad range of hazards in clinical and laboratory settings. Hepatitis, instead of being singled out, was being normalized.

While Rosenheim may have been absolutely fair and correct to attempt to stabilize the perception of hepatitis B and bring it within the fold of normal hospital infection hazards, in order to avoid over-dramatization, the committee omitted two potentially valuable comparative dimensions, at least in its report.[25] One of these would be a comparison of the hepatitis outbreaks with those of other diseases regarded as hospital infections such as puerperal fever or streptococcal infections. The framework of thinking about hepatitis B referred repeatedly to the hospital setting, as in the recommendation to reduce transfusions for dialysis patients to

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[23] Dr Roger Williams, interview, 14 December 1992.

[24] Rosenheim Report, p. v.

[25] Again, the group's deliberations, which may have included a review of these elements, cannot be considered until the unpublished records are available.

a minimum, on the assumption that this was the commonest route of infection in the first instance. Why then the lack of comparison with other hospital infections, and the 'lessons of history' to be learned from them? Rosenheim pointed out that other such infections had been met and conquered in the past, so presumably hepatitis would be, but gave no details of these past conquests. Perhaps there was a reluctance to admit that these other problems had been very serious until specific drugs had been found to counter them: sulphonamides for puerperal fever, penicillin and other antibiotics for streptococcus.

Past incidents involving hepatitis constitute another area for comparative insights, also overlooked by the committee. Post-transfusion hepatitis was apparently the predominant form of serum hepatitis with which the group and their informants were familiar; but this affected individuals separated in space and time, rather than causing 'outbreaks'. Those who recalled hepatitis outbreaks among troops during the Second World War perhaps derived some comfort from the fact that the renal unit outbreaks affected lesser numbers absolutely (though possibly a higher proportion of the given population). The lesson learned from arsenic-therapy jaundice, that syringes could transmit hepatitis,[26] was indirectly applied in the call for disposable syringes to be used.

Other avenues might have been explored. The appearance of

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[26] A lesson apparently relearned in the 1960s: see Chapter 6, n. 30.

serum hepatitis in venereal disease treatment might have suggested a venereal route for transmission. The commonest form of syringe transmission, by illicit drug injection, was recognized by this time but scarcely discussed - despite the finding in the Royal Free report that the source of the hepatitis outbreak there appeared to have been a drug user, who shared syringes with others before admission to the dialysis unit.[27] In the past, serum hepatitis had afflicted groups herded together, to undergo vaccinations or treatments (shipyard workers, troops, mental hospital inmates - and at one stage it was thought munitions workers), but as the committee noted, it had rarely appeared as a problem in hospital contexts.[28]

The Rosenheim group absorbed from the various units and the PHLS the message that strict precautions to avoid contact with patients' blood and other bodily secretions should be taken by all staff working in dialysis units; they also emphasized isolation, not only in the sense of isolation units for treatment of hepatitis carriers within the units, but working towards a situation where each patient should perform his or her own dialysis, in hospital if necessary and preferably as soon as possible at home. Ideally every chronic renal failure patient would receive a kidney transplant, obviating the need for further dialysis, but since this could not be achieved in the forseeable future, the majority should move to home dialysis. There was hope of developing a disposable dialyser

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[27] Knight et al, 'Hepatitis-associated antigen', 605.

[28] Rosenheim Report, p. 12.

(cost was not discussed); this would clearly reduce the infection risk, just as the currently available disposable syringe had done.

If hygiene precautions were one important part of the Rosenheim message, another was the identification of the 'culprit' as an agent associated with Australia antigen or antibody (they were unclear on this), enabling far more precise methods of separation and exclusion of infected persons to be brought into play than previously possible. Patients and staff were to be regularly screened, infectious patients excluded from the main unit and movement between units to be controlled. Staff were to be screened before working in renal units and excluded if positive for the Australia antigen. It was not made clear what would then be their fate - whether they could work elsewhere in the hospital or not. Those staff already working in the units who developed suspicious symptoms would be off duty until they exhibited and cleared the antigen or turned out to have some other ailment.

These recommendations for screening and separation or exclusion of patients and staff carrying the Australia antigen partly coincide with suggestions in published papers describing outbreaks in particular renal units, and partly appear to have been based on the work of the PHLS team. Sir James Howie wrote to Polakoff in the autumn of 1970, shortly following the establishment of the Rosenheim group, saying that he wanted a written report on her work by the following

Monday. Polakoff and Cossart managed to meet the deadline, working like Stakhanovites over the weekend, and Sir James was apparently 'charmed' by their report.[29] The Rosenheim conclusions were heavily influenced by the Polakoff/Cossart explanation of the connection between Australia antigen and the renal unit outbreaks, and equally by their views on screening and isolation. Polakoff was called to give evidence in person later, but was ill with overwork and recalls little of the meeting; she needed three weeks bed-rest to recover.

Although the PHLS approach might be thought of as a central response, it must be remembered that Polakoff and Cossart were monitoring data from, and collating action taken by, many of the renal units that had suffered outbreaks. In a sense they had started the information gathering process that Rosenheim was engaged upon, two years ahead of Rosenheim. From the centre, the PHLS and Rosenheim disseminated to all renal units an amalgam of 'best practice' garnered from local units and laboratories, informed by discussions with UK experts and by monitoring internationally published literature. Rosenheim achieved a policy on screening and exclusion by a synthesis of scattered efforts, largely, it is argued here, on the basis of PHLS work, which also ensured follow-up via surveillance.

The continued monitoring of the renal units was paying off, even by mid-1972 when the Rosenheim group reported and its recommendations were circulated to all renal dialysis and

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[29] Polakoff, interview.

transplantation units.[30] Now the policy of screening and exclusion was official and nationwide, local differences of interpretation were more readily overridden, and Polakoff and Cossart were able to secure almost total cooperation with their programme of monitoring hepatitis.[31] They themselves, according to Polakoff, 'couldn't beliveve how well it worked', but by 1975 they had cracked the problem and there were no further hepatitis outbreaks in renal units in the UK.[32] Perhaps the severity of the Edinburgh outbreak of 1969-1971 had also played a part in convincing all workers in renal units to observe strict precautions. But the setting of a central policy by Rosenheim, and above all the role of the PHLS, would appear to have been crucial.

In other countries where similar action was not taken, hepatitis B remained a hazard in renal units far longer than in the UK. For example, in France it was reported that as many as half the staff in renal units were infected with hepatitis B by 1978.[33] In America, too, renal units continued

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[30] Public Health Laboratory Service, 'Decrease in the incidence of hepatitis in dialysis units associated with prevention programme', British Medical Journal, 1974 (4), 751-54. [Report prepared by S. Polakoff.]

[31] Almost, but not quite total - for example, one London hospital resisted the request to have its patients and staff tested, until they had an overt case of hepatitis: D. S. Dane, interview, 16 August 1992.

[32] Polakoff, interview. See also: S. Polakoff, 'Hepatitis B in retreat from dialysis units in United Kingdom in 1973', British Medical Journal, 1976 (1), 1579-81.

[33] P. Maupas, A. Goudeau, et al, 'Hepatitis B vaccine: efficacy in high-risk settings, a two-year study', Inter-virology, 10 (1978), 196-208, gave figures of hepatitis B infection of 40-60 per cent among patients and 50 per cent among staff each year in French renal dialysis units. An informant who worked

to operate with a high level of hepatitis B transmission through the 1970s.[34] In other countries with a screening policy, such as the Netherlands, hepatitis was checked much earlier.[35] The difference seems to have been mainly a matter of the organization of health services, particularly public health laboratories, in each country: Britain's advantage lay in the central PHLS's link with peripheral laboratories. Quite possibly the PHLS network itself would not have been sufficient without the efforts made by two workers at the centre to contact key people in all the hospitals involved.

The aftermath of the renal unit hepatitis outbreaks

I would argue that the hepatitis outbreaks in renal units had a far wider and deeper impact than the numbers involved might indicate; an impact that appears to have gone largely unrecorded, although it emerges strongly from oral sources. This impact was long lasting, despite the 'normalizing' message of Rosenheim. Clearly, there were immediate changes in policy and practice relating to infection prevention in renal units themselves, as a result of the Rosenheim Report and the efforts of the PHLS described above. There were associated effects in the handling of samples of blood and

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in such a unit during the 1970s described immunoglobulin injections administered to all staff at three-monthly intervals as a painful and not very effective: A-M. Moulin, personal communication, 19 Nov 1993.

[34] D. Surgenor, T. C. Chalmers et al, 'Clinical trials of hepatitis immune globulin', New England Journal of Medicine, 293 (1975), 1060-2.

[35] F. M. Parsons et al, Proceedings of the European Dialysis and Transplant Association, 11 (1974).

serum in clinical laboratories. One informant likened the fear inspired by the hepatitis outbreaks to that engendered by AIDS some fifteen years later.[36] Not only would samples from patients with the disease be handled as potentially lethal substances, but all blood samples acquired a new aura of risk.[37] Simultaneously, the view of the risks that doctors and nurses ran in the course of their routine hospital duties also altered, perhaps to a degree corresponding with proximity to one of the centres that suffered an outbreak.

Fictional sources must be used with care, but there is one which must be acknowledged in this context, for it sheds a baleful if tangential light on 'the aftermath' of the renal unit outbreaks. In The Houseman's Tale, a novel loosely based on the Edinburgh hepatitis B outbreak, Colin Douglas uses a device borrowed from the detective genre: he lays a trail of clues for observant eyes throughout the book, hinting that junior hospital doctors are exposed to the deadly 'serum hepatitis' in the course of their duties.[38] Their routine contact with the blood and bodily secretions of dozens of patients, any of whom might be an unknown carrier, puts them in the front line. But at the denouement, the culprit is revealed to be something completely different - though the clues were there for even more canny eyes - a nurse called Maggie who had contracted hepatitis B in the renal unit has

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[36] B. Gee, interview, 21 June 1991.

[37] Responses including changes in handling of blood in clinical laboratories will be further explored in Chapter 7.

[38] C. Douglas, The Houseman's Tale (London: Hutchinson, 1975)

given it to at least three doctors she subsequently slept with. One of these dies at the beginning of the book, a second at the end (as in good detective stories, there are two corpses), while the third survives to become the hero of a whole series of 'doctor' novels.

The sense of dread induced by acute hepatitis is conveyed in a description of precautions taken in the Isolation Unit:

> [Mac speaks to his friend Campbell, the hero:] 'You know Ivor, the SHO here? Came at me for blood dressed like a deep-sea diver: boots, gauntlets, a thing like a welder's mask on his face and funny paper hat like yours. It made me feel I wasn't nice to know.'[39]

Later, lying ill in the next cubicle, Campbell hears Mac has died, and although familiar with death on the wards, is devastated:

> Here [death] was brazen and fierce and had just snatched someone with whom he had a conversation to finish: it was an obscene and extravagant assertion of death as the ancients had known it - random, sudden and implacable, the seizer of all men, guided by blind fate.[40]

Campbell is scared about his own fate, but comforts himself that this disease was 'nasty but it was not new or unknown'. Unlike Maggie, who commits suicide when she realises what has happened (echoes of a Victorian novel), Campbell is lucky enough to clear the virus from his system and continue his life, and his career.

In The Houseman's Tale, the Edinburgh outbreak has spread fictionally into the hospital. The device of using a nurse as the agent of transmission has been critically analysed in

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[39] Ibid, p. 146.

[40] Ibid, p. 161.

relation to AIDS and gender issues.[41] It is certainly striking that in the early 1970s, when few doctors were aware of the sexual route of transmission for hepatitis B, this author wove it so tellingly into his plot. The reference to serum hepatitis as 'not new or unknown' bears comparison with Rosenheim's normalizing rhetoric; it also underlines for us the contrast with AIDS, when the unknown-ness of the disease was one of its most terrifying aspects. On the other hand, despite this phrase, the whole thrust of Douglas's portrayal of hepatitis B in The Houseman's Tale shows it as a terrifying and intractable disease. Exposure to it was one of the more severe of the many trials that mark the transition of the junior doctor from callow youth to medical manhood: those who succumbed were heroes, those who survived were heroes. But - in this version - the nurse who unwittingly passes on infection to three doctors is an object of blame and disgust.

It would certainly be unwise to generalize from a reading of this particular account; there is evidence elsewhere of sympathy between members of different professional groups within the health care arena over the issue of hepatitis B infection. One Rosenheim witness spoke of being moved by accounts of young doctors and nurses dying. The same witness suggested that doctors were cautious when it came to treating drug addicts who might be hepatitis B carriers.[42] The renal unit outbreaks possibly enhanced an already-existing

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[41] P. A. Treichler, 'AIDS, gender and biomedical discourse: current contests for meaning', in Fee and Fox, AIDS: the burdens of history, pp. 190-266, esp. pp. 190-2.

[42] Williams, interview.

perception of certain categories of patients as hazardous. Here is a description from the renal unit setting which, despite the constraints of medical journalese, succeeds in conveying the problems that could be encountered when a patient was uncooperative:

> Case P4 had developed renal failure with a right renal carbuncle and pyelonephritis due to septicaemia from self-administration of methadone ... Personality and psychological difficulties greatly complicated treatment in this man. Routine dialysis, with access to the bloodstream by arteriovenous fistula, was frequently disrupted, resulting in blood spillage and staff intervention, with contamination.[43]

In another context, for instance, a discussion of samples in test tubes, the term 'contamination' could be used in an unemotive scientific way, but here it bears an emotional connotation: staff who are forced to intervene are exposed to danger from the spilled blood of a drug addict.

Conclusions

This chapter described the hepatitis outbreaks in renal dialysis units in Britain in the period 1965-71, which are seen to have had a major impact on the way that the medical profession and policy makers constructed hepatitis B. Now seen primarily as an occupational hazard of health workers, hepatitis B was regarded as a far more threatening hazard after this episode than before. On the other hand, this chapter has also described how this dramatic new risk of hepatitis was successfully contained after 1972, when the Rosenheim committee reported.

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[43] Knight et al, 'Hepatitis-associated antigen', 605.

How far was this success attributable to the Australia antigen discovery and the availability of a test for hepatitis B, for the first time, from 1969/1970? Clearly these scientific developments provided very important tools. The timing of their application was almost certainly influenced by the renal unit outbreaks; had these not occurred, there would probably have been a longer period of exploration, of testing the tests, before implementation. Had a test not become available, it seems renal units would still have continued in operation, although greater changes in mode of operation might have been seen, with patients treated in spatially separated cubicles, and home dialysis favoured.[44] Since the system of testing introduced in this country was not applied in many other countries, or not applied so soon, it cannot be assumed as the inevitable 'logical' response.[45]

In view of the enormous impact of the renal unit outbreaks, in reinforcing the construction of hepatitis B as a (blood associated) hospital infection and as an occupational hazard of health workers, the 'normalizing' efforts of the Rosenheim committee must be seen as significant. There are implications for Chapter 7, which shows health and safety of most health

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[44] Britain actually moved towards home dialysis earlier, faster and further than many other European countries despite its success in containing hepatitis in renal units - other factors partly account for this shift.

[45] See literature on different rates of diffusion of new medical technologies, for example: Stocking, 'Factors affecting diffusion'; chapter on 'Medical innovation' in J. R. Hollingsworth, J. Hage and R. A. Hanneman, State intervention in medical care. Consequences for Britain, France, Sweden and the United States, 1890-1970 (Ithaca and London: Cornell University Press, 1990), pp. 112-36.

workers, in relation to hepatitis B, tackled in the 1970s by hygiene precautions and compensation provisions, rather than by testing (as in renal units); and by extrapolation, for Chapter 8 also, where health and safety policies set the agenda for a limited vaccine policy.

Perhaps the most important feature of the response to the renal unit outbreaks, for the analysis of policy-making, is not so much the arrival of the Australia antigen test, or the setting up of advisory groups to make recommendations, but rather the balance between central co-ordination and local initiative. Health staff confronted with the problems were working out their own solutions ahead of the establishment of a central advisory groups by the DHSS, so that the experts sitting on this group were able to draw on both positive and negative experience at the 'coal face'. There was very practical evidence of the utility of the Australia antigen test in containing the hepatitis outbreak at Royal Free, for example. The role of the central PHLS and the national network of public health laboratories was also crucial. There are analogies in the case of clearing the blood supply of hepatitis B, the subject of the next chapter.

CHAPTER 5: HEPATITIS IN BLOOD AND BLOOD PRODUCTS: ISSUES OF ALTRUISM AND SELF-SUFFICIENCY [c1972-1987]

From the earliest point when hepatitis B began to be identified as a separate disease, during the war, it had been closely associated with blood and plasma and in the postwar period it was seen as a major hazard of blood transfusion. The Australia antigen test was rapidly grasped as a means to control this hazard - perhaps more rapidly than would otherwise have been the case, had not the renal unit outbreaks forced hepatitis B up the health policy agenda at the end of the 1960s. The science of hepatitis B and the implications of the Australia antigen finding were subject to much excited discussion around this time, of course, but the mood was rather one of opening up an area of investigation, than of having found the answers.[1] At the same time as establishing the Rosenheim Committee, the Department of Health set up a parallel committee on testing blood, the Maycock Committee, the subject of the first part of this chapter.

The previous chapter warned against seeing the application of Australia antigen testing to the problem of hepatitis B in renal units as the whole explanation of the solution. Organizational structures and initiative were as important as central policy. This is clearly true of testing blood too, and here we have to consider additional caveats to the notion

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[1] See for example: 'Australia antigen and hepatitis', leading article, Lancet, 1969 (ii), 143-4; 'Hepatitis virus', leading article, Lancet, 1969 (ii), 577-8; oral evidence is not particularly helpful here, tending to give an over-positive interpretation of applications of the finding.

of 'solution'. While testing effected a valuable reduction in rates of hepatitis B following whole blood transfusion, it had far less impact where blood products such as Factor VIII[2] were concerned. The two main variables here, pooling and source of the raw material (plasma), will be discussed in relation to the influential work of Richard Titmuss on this subject; for Titmuss, donor altruism was the greatest guarantee of safety, and payment of the donor compromised safety. The remainder of the chapter traces the failure to remove the infection hazard from a small but important area of the blood supply: blood products for haemophiliacs.

During the 1970s, a large number of haemophiliacs in England and Wales became infected with hepatitis, as the use of Factor VIII increased.[3] Few died and it seems the risk was subordinate to other considerations, of cost and convenience, in choice of products. In any case, the organization of transfusion services was not geared to meeting the ever-increasing demand, and commercial Factor VIII, mainly from America, filled the gap throughout the 1970s and into the 1980s. Although expert opinion was divided on the question of source versus pool size in determining hepatitis risk - and NHS products used large pools - the inexporable rise in hepatitis rates among haemophiliacs played a part in the drive

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[2] A concentrated plasma fraction contained the missing clotting factor; there was also factor IX for a rarer form of haemophilia. There were roughly 4,500 haemophiliacs in the UK at the time the clotting factors were introduced.

[3] Some of this infection was hepatitis B, some was non-A non-B hepatitis, a diagnosis of exclusion as no test was available.

to seek self-sufficiency in blood products.[4] Despite government promises to upgrade the central Blood Products Laboratory, from 1976 onwards, upgrading and self-sufficiency in blood products was not achieved until ten years later, by which time many haemophiliacs had been infected with HIV/AIDS as well as hepatitis.

The Maycock committee and its successors

During the postwar period, the hepatitis risk associated with transfusion had been monitored by the MRC, as well as the blood transfusion service and the central Blood Products Laboratory, at Elstree near London. A 1954 MRC study on hepatitis after blood and plasma tranfusion reported a rate of 0.36 per cent for whole blood and 1.17 per cent for plasma.[5] Subsequently an MRC Working Party on Post-transfusion Hepatitis was established, to meet intermittently, with Zuckerman of LSHTM as secretary from 1966, and Sir William Maycock, Director of BPL, as chairman. Zuckerman felt that he had stimulated MRC interest in hepatitis,[6] which may be partly the case; but the concern which had developed during the war had probably never faded completely. Figures such as Mollison, Professor of Haematology at St Mary's Hospital

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[4] An aim achieved north of the border, in Scotland, before 1980, with a consequent reduction in infection hazard.

[5] 'Homologous serum jaundice after transfusion of whole blood, dried small-pool plasma, dried irradiated plasma, and kaolin-treated filtered liquid plasma', Lancet, 1954 (i), 1328-9; this was a report of a survey by an ad hoc group on behalf of the MRC, Ministry of Health, and Department of Health for Scotland.

[6] A. J. Zuckerman, interview, 8 June 1992.

Medical School,[7] and Maycock, head of BPL and adviser on blood transfusion, were clearly aware of the problem.

Through its longstanding connections with the MRC on blood transfusion policy, the Department of Health was primed for action when rumours of the link between Australia antigen and hepatitis B hardened into high probability, and tests became available. In 1970, at the same time as setting up the Rosenheim committee on hepatitis in renal units, the DHSS also established a committee on Australia antigen testing in the blood supply under Maycock. Reporting in 1972,[8] the Maycock Committee laid down ground rules for hepatitis testing of all blood, which seem uncontroversial in retrospect. But the scientific evidence on which the committee based its decisions had shifted and accumulated with unprecedented speed during the two years it had been sitting, so that technical choices on which sort of test to use changed from one month to another. With a national network of regional transfusion centres administering about two million donations a year, the organization and financing of testing appeared at the time as formidable tasks.

Several members of the Maycock committee are familiar names elsewhere in this history: F. O. MacCallum, the virologist who had led the wartime jaundice research team, now with the PHLS at the Radcliffe Infirmary, Oxford; A. J. Zuckerman,

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[7] Author of Blood transfusion in clinical medicine (cited in Chapter 4): 1st edition 1951, 2nd 1956, etc; Director of MRC Experimental Haematology Unit at St Mary's.

[8] Maycock Report.

virologist at the London School of Hygiene and Tropical Medicine; D. S. Dane, virologist at the Middlesex Hospital, London; and Yvonne Cossart of the Central PHLS Virus Reference Laboratory at Colindale. These four, plus five of the remaining six members of the committee, and the chairman, were all Fellows of the Royal College of Pathologists. Only one member represented the 'rank and file' of face workers in daily contact with the process of testing blood, the laboratory technicians: C. H. Collins, a Fellow of the Institute of Medical Laboratory Technicians.[9] The Maycock and Rosenheim committees liaised closely, but Maycock took no live evidence, relying instead on papers 'from a wide variety of sources at home and abroad including WHO', and information passed on by contacts of committee members.[10]

The MRC study of 1954 and another in progress in 1970-72 led the Maycock committee to estimate that hepatitis with jaundice occurred in about 0.2 per cent of transfusion recipients but anicteric hepatitis (without jaundice and therefore not diagnosed) possibly in about 4-5 per cent.[11] Testing should reduce this to about a quarter of the present incidence,

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[9] There were also secretaries to the committee, two of whom were provided by the DHSS.

[10] Maycock Report, p. 1; the International Society of Haematology Symposium, 1970, was another valued input.

[11] Ibid, p.2. See also: Lendrum, R., Walker, J. G. et al, 'Post-transfusion hepatitis in a London hospital: results of a two-year prospective study', Report to the MRC Blood Transfusion Research Committee by the MRC Working Party on Post-Transfusion Hepatitis, Journal of Hygiene (Cambridge), 73 (1974), 173-188, for estimate of morbidity and mortality at around 27 cases of hepatitis, including 8 deaths, per 10,000 units of blood transfused in patients receiving blood only.

lessening the burden on the NHS - as well as individual suffering - and was therefore recommended. But the committee sought a balance between safety, and ensuring that an adequate supply of blood was maintained. With views about the Australia antigen in a state of flux, there was uncertainty over serological evidence of past infection - or rather, how far to regard this as a danger.[12] There was a dilemma over whether to exclude donors found to be antibody positive, as well as those who were antigen positive; Maycock recommended exclusion of both on the basis of relatively insensitive tests.[13] Regional blood transfusion centres might choose a more sensitive test, such as radioimmunoassay, which could reveal a large number of donors with low levels of antibody; Maycock recommended against exclusion of such donors, recognizing that such a step might seriously reduce donor panel size. There was no consensus at this point on the likely infectivity of people whose blood carried antibody without detectable antigen.

The task of the Maycock committee was undoubtedly facilitated by the work of a few regional transfusion centres that had previously started Australia antigen testing, providing a limited amount of data on the likely numbers of donors in different categories (antigen or antibody positive) using different tests. Maycock made special mention of Glasgow and

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[12] Finding the evidence, i.e. presence of antibodies, required a mirror image of the procedure for antigen testing, and was possible once HBsAg testing itself was available.

[13] Immunodiffusion, immunoelectroosmophoresis, complement fixation: the point is, these would only pick up those with high levels of antigen or antibody.

West of Scotland, and Sheffield BTCs. Another centre which introduced testing early was North London BTC; its Director, Dr A. Cleghorn, decided to exclude only those donors found to be antigen positive, on the grounds that antibody in the blood indicated successful resistance to the virus and almost certainly a non-infective state. Dane, who sat on the Maycock committee, agreed with Cleghorn's policy, but this was the minority interpretation, until gradually other BTCs came round to the same view.[14] There existed for some time a situation where North London BTC, contrary to the recommendations of Maycock, was supplying blood which had tested positive for hepatitis B antibody (but negative for antigen): in the view of some experts running a risk of infecting patients. Cleghorn, Dane and their colleagues, on the other hand, were confident on the basis of the tests they were using that their own interpretation was correct, and their procedures safe.

Advance testing by some regional BTCs, and their different policies following the 1972 Maycock recommendations, illustrate the semi-autonomy of the regions which is such a striking characteristic of many services within the apparently centralized British NHS. Universal screening of all blood donations was achieved within a few months of the Maycock report, but choice of tests used, and which donors to exclude, varied. From two points of view, scientific and financial, a greater degree of central co-ordination might have had advantages. Had evaluation of tests been organized centrally, large-scale results could have been amassed and assessed

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[14] D. S. Dane, interview, 6 August 1992.

rapidly. Since antibody testing added to costs, a more rapid recognition that it was superfluous could have saved money. But the entrenched system of local control by the consultant in charge of ward or laboratory extended to the BTCs; central policy here, as in other areas, laid down guidelines for safety and left much leeway for local initiative.

This is not to belittle the achievements of the UK blood transfusion service in rapidly clearing the blood supply of a very large percentage of hepatitis B. In some centres, notably Glasgow and North London BTCs, as well as the central BPL, considerable effort went into developing improved tests. Percentage returns diminished sharply, that is, the number of cases of hepatitis B prevented by improved testing became fewer with each improvement, so that costs had to be low to justify research and development expenditure.[15] At BPL, a research scientist and a technician, in alliance with Dane's Middlesex Hospital team, and North London BTC, evolved a test that became widely adopted for use in the NHS, reputedly saving the service £10 million compared with commercial products.[16] The wonder is not that BPL made a successful test, saving the NHS millions of pounds, but rather that most tests have been bought in from commercial companies like the Wellcome Foundation.[17] Why does the NHS have to rely so

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[15] J. Barbara, Microbiology in blood transfusion (Bristol, London, Boston: Wright-PSG, 1983), pp. 24-5.

[16] See Chapter 6 for more detailed account.

[17] Wellcome's 'Hepatest' was developed in collaboration with some of the researchers involved in the BPL test; see Chapter 6 again.

heavily on pharmaceutical companies for its requirements? This question becomes even more urgent when we turn to look at blood products.

It remains to take this account of hepatitis in the blood transfusion service through the 1970s by recording that the Maycock report of 1972 was followed by updates in 1975 and 1981.[18] Essentially the second report, in 1975, responded to refinements in testing and in views of carrier status.[19] Donors with antibody were to be retained on the panel, those with a history of jaundice need no longer be excluded; a particular type of test was recommended;[20] there was more emphasis on testing BTC staff; and on extracting specific anti-hepatitis B immunoglobulin from donors with sufficient antibody. The central PHLS was asked to supply reagents to regional BTCs and reference centres. Epidemiological work under the central PHLS should be supplemented by all testing centres letting each other know immediately of cases of hepatitis caused by blood or blood products. Differential notification of B and other types of hepatitis should be reconsidered by the DHSS.

The advisory group which prepared the 1981 report, in addition to a different chairman, had a substantial change in personnel

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[18] Maycock remained as chair for the 1975 group; the group which reported in 1981 was chaired by W. J. Jenkins.

[19] DHSS, Second report of the advisory group on testing for the presence of hepatitis B surface antigen and its antibody (London: HMSO, 1975)

[20] Reversed passive haemagglutination rather than counter-immunoelectrophoresis.

- only four members of the 1975 group remained.[21] Elise Vandervelde replaced Yvonne Cossart (with whom she worked closely); Dame Sheila Sherlock, Professor of Medicine at Royal Free Hospital Medical School, the doyenne of liver function testing, was an obvious choice; Dr E. A. C. Follett of Glasgow Regional Virus Laboratory and T. E. Cleghorn of North London BTC were other additions. For the first time the group brought out its report using the term 'hepatitis B surface' antigen and antibody, abandoning the previous 'Australia antigen' terminology. New standards of sensitivity were set for tests, indeed a British standard of HBsAg was available to suitable laboratories.[22] Debates recently opened up in the scientific community were reflected in negative recommendations: against screening for the core antigen (it seemed adequate to screen for the surface antigen only as a proxy for infectivity); and against the use of liver function tests for general screening of blood donors.[23] Now, as concern over non-A, non-B hepatitis was rising, hospitals were asked to single out suspected cases; research into the extent of non-A, non-B hepatitis viruses 'should be undertaken in the

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[21] DHSS, Third report of the advisory group on testing for the presence of hepatitis B surface antigen and its antibody, 1981. (Typescript)

[22] To be designated as 'suitable', a laboratory had to demonstrate awareness of the need for safe handling of HBsAg.

[23] As Sherlock was the expert on liver function tests and sat on this advisory group, it can be assumed she supported this recommendation. Liver function tests could detect raised transaminase levels which might indicate hepatitis in its early stages (when it would not be detectable by antigen testing) but might be due to other causes; some 3 per cent of donors could be ruled out if these tests were applied, without appreciable clinical benefit: Third report on testing for hepatitis, p. 5.

UK'.[24] Other fresh recommendations included the setting up of a panel of experts to assess new hepatitis tests; and training programmes to be established by the blood transfusion service for staff who carried out hepatitis testing.[25]

Haemophiliacs and risk factors in blood products

It may be recalled from chapter 3 that haemophiliacs figured prominently among subjects whose blood contained antibodies which reacted with Australia antigen in the early experimental days, when Blumberg and others were fitting together the pieces of the puzzle. Samples of blood from haemophiliacs also proved valuable in EM research, when the antigen and then the virus were visualised. Haemophiliacs were useful in this way because they received multiple tranfusions, when little else could be done to counter the bleeding they suffered from.[26] Many other means of stemming the flow of blood were tried - for example, there was a vogue for snake venom in the 1940s[27] - but there was no really effective treatment until the isolation of clotting factors: Factor VIII for haemophilia A and Factor IX for haemophilia B, which became available for treatment in the 1960s.

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[24] Ibid, p. 8.

[25] This may reflect technicians' protests around 1980 over DHSS attempts to downgrade the hazard rating of hepatitis B: see Chapter 7.

[26] Multi-transfused patients were likely to have been exposed to hepatitis B infection; their blood would then carry either antigen or antibody.

[27] D. Bateman, 'The good bleed guide: a patient's story', Social History of Medicine, 7 (1994), 115-33, esp.124.

Clotting factors must have appeared as one of those miracles of modern medicine that transform an intractable problem overnight, in this case freeing haemophiliacs from long periods of hospitalisation, and increasing life expectancy. It was a great advance in the treatment of haemophilia, but like many other new medical technologies, it brought new problems, in this case especially an intensified risk of hepatitis infection. As Factor VIII became a home-use, everyday treatment, the hepatitis risk was further multiplied; but hepatitis infection was often covert and unrecognized. In any case, as with other innovations, the gains outweighed the side-effects, in most contemporaries' view.

Besides the pool size, the social nature of the donation was another important determinant of safety in the blood supply - the most important in the view of at least one authority. Richard Titmuss, in his 1970 study of blood and policy, discussed the social dimensions of blood and plasma production at length, but the argument can be summarized simply: was the donor paid or not?[28] At that time, the rate of hepatitis associated with blood transfusion was much higher in countries where many donors were paid, such as the US and Japan, than it was in Britain, where blood donors were entirely voluntary and unpaid.[29] Sparse statistics were available in the 1960s, but rates appeared to be in the order of 10 to 25 per cent in Japan, compared with under 0.2 per cent in Britain, for whole

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[28] Titmuss, Gift relationship), p.157; actually his summary is not quite so simple.

[29] There was a much higher prevalence of hepatitis B in Japan than in Britain but Titmuss took this into account.

blood transfusion.[30] Various US studies indicated a much higher rate where the source of blood was paid donors. Quite apart from any differences in prevalence of hepatitis carriers in different populations, Titmuss indicated the sale of blood was crucial:

> These disastrously high rates in Japan have been attributed almost entirely to the fact that approximately 98 per cent of all blood is bought and sold ... "professional blood sellers" - popularly known as "tako" (octopus) - are said to visit two commercial banks a day, selling 200cc. at each bank. Before each visit they gulp a concoction of iron filings in salt water, and eat spinach and dried sardines, in the belief that this will thicken their blood.[31]

Titmuss noted that the American Ambassador had contracted hepatitis from blood transfusions in a Tokyo hospital in 1964. Ironically, the commercialism in the blood supply seemed to stem from a decision to pay donors in Japan in order to supply blood to Americans in Korea in 1951; but since then, with rising commercialization, there had developed a growing shortage of blood.

Another point of special relevance in the manufacture of blood products was that plasma donors could make more frequent donations than those giving whole blood. In plasmapheresis, blood was taken from the donor, most of the plasma extracted, and the red cells returned to the donor, in one process. If a plasma donor carried hepatitis B, then the ability to donate more frequently increased the chances of passing the infection to more recipients. But why was the altruistic motive in

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[30] Titmuss, Gift relationship, pp. 154-5.

[31] Ibid, p. 156, with quote from: 'Blood donors in Japan', Transfusion, 3 (1963), 213.

giving blood or plasma a safeguard? What happened when giving blood became a commercial transaction?

In all cases of blood and plasma donation, processing and distribution, Titmuss argued, the crucial factors are trust and truthfulness: trust must be displayed by those taking, buying or receiving the blood or blood product, and in return they expect truthfulness from the donor, salesperson or medical personnel giving the blood or blood product. At each stage, trust and truthfulness could be compromised by a commercial transaction. The switch from an altruistic motive for giving blood to one of financial gain attracted a higher proportion of indigent people, less healthy and perhaps more secretive about their health record than most voluntary donors. Similarly, companies promoting sales of blood products were sometimes dishonest concerning the origins of the blood, and more willing to overlook slack health checks on donors. In the States, the growing number of profit-making hospitals often paid less attention to quality and safety controls than to the price of commercially-produced blood products for which they provided an expanding market - as evidenced by the higher rates of post transfusion hepatitis in such hospitals.[32]

With the introduction of Australia antigen testing, the situation changed dramatically for whole blood, but not for blood products. Titmuss, though aware of the possibility of a

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[32] For an expansion and updating of this argument with data on the US, see: P. Hagan, Blood: gift or merchandise? (New York: Alan Liss, 1982)

test for serum hepatitis, was unsure of its close imminence when he wrote in 1970:

> The absence of a scientific check on quality and safety means that the subsequent biological condition of those who receive blood constitutes the ultimate test of whether the virus was present in the donation; in effect, therefore, the patient is the laboratory for testing the quality of 'the gift'.[33]

The advent of a test for hepatitis B, albeit initially a rather unreliable one, made possible a shift in the site of the laboratory from the patient's body to the blood transfusion centres, blood banks in the US, or reference laboratories. Both in the more commercial environment in the US, and in the UK, this was achieved rapidly with central policy being drawn up on the basis of expert advice, then imposed throughout the system.

If we looked at a graph of the number of hepatitis B carriers found among blood donors, or cases of post transfusion hepatitis B, in the 1970s and 1980s, we would observe a rapid fall after the introduction of testing in 1972 and a gradual whittling away of the residue thereafter.[34] Does this mean that Titmuss's emphasis on trust and truthfulness was bypassed, dismissed into irrelevance by the laboratory test which removed the risk from the previous test site, the patient's body? No, on at least two counts. First, patients still needed to trust the doctor or nurse administering the transfusion or blood product, and behind them the whole array of laboratory technicians, manufacturers of tests, and

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[33] Titmuss, Gift relationship, pp. 142-3.

[34] Barbara, Microbiology in blood transfusion, pp. 25, 42.

suppliers of blood products. Second, a hepatitis risk remained: a minimal risk of hepatitis B, since samples from a donor in the early stage of incubation might test negative but still carry infection (a risk magnified by pooling); and a larger risk of non-A, non-B hepatitis, which was still untestable. As one problem was brought under control, another problem emerged, or so it seemed: of course, non-A, non-B hepatitis had been there all along and was merely revealed by the new mastery over hepatitis B. And as we now know, by the late 1970s or early 1980s (depending which area you consider) a further problem was lurking in the blood supply: HIV/AIDS.

Safety, cost and convenience in choice of blood products

For technical reasons already explained (removal of multiple donations from donors by plasmapheresis, combined with pooling large numbers of plasma donations to make plasma fractions) blood products such as Factor VIII were much more liable to transmit hepatitis (B or, more likely, non-A, non-B), than simple blood or plasma transfusions. Thus, for recipients of blood products, donor and manufacturer truthfulness remained especially important. Yet, in the US, the use of paid donors remained legal for plasmapheresis, probably because of the high degree of involvement of commercial blood banks and pharmaceutical companies in manufacturing blood products. Paid donors meant an increased risk of hepatitis in the product. Companies trawled third world countries for the raw materials; plasma was imported into Europe and the US from countries with

a high rate of hepatitis.[35] In the UK, where all blood and plasma donors were unpaid, home-produced blood products afforded a safer supply than imported, commercially produced products - though the degree of safety was debatable, because of the large pool size used in manufacture. In any case, hepatitis risk was not at the forefront of policy concerns: other factors were to decide whether Britain opted for use of imported blood products.

At the beginning of the 1970s, when it was still a relatively new treatment, Britain used mainly home-produced Factor VIII.[36] Concerns over safety focussed on pool size and method of manufacture, rather than whether the donor was paid or not. Besides safety, there was concern to predict the amount and type of Factor VIII likely to be needed by haemophiliacs as the treatment became routine; and to find ways of stepping up production. There was also a strong movement towards enabling haemophiliacs to use Factor VIII at home, rather than limit it to hospital use.

These issues are reflected in the report of an MRC committee, which sat between 1969 and 1972, looking at the use of Factor VIII made from various sorts of concentrate in the UK.[37] The

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[35] Bateman, 'Good bleed guide'; Hagan, Blood: gift or merchandise?

[36] This was mainly cryoprecipitate, given in hospitals; increased home treatment led to greater demand for freeze-dried concentrate, imported when UK supplies were inadequate.

[37] R. Biggs, C. R. C. Rizza et al, 'Factor VIII concentrates made in the United Kingdom and the treatment of haemophilia based on studies made during 1969-72', Report of the MRC's Blood Transfusion Research Committee Working Party on the

group came to the conclusion that: '... within the next few years a great effort should be made to increase the amount of plasma which is fractionated in the United Kingdom.'[38] They saw a need to boost the amount of one type of concentrate (freeze-dried) as opposed to another (cryoprecipitate), to facilitate home treatment - the former being easier for the haemophiliac to reconsitute and self-administer. The working party thought that the incidence of jaundice depended more on dose than on the type of donor or size of pool, and noted that antigen testing should in any case reduce the danger of hepatitis infection. The rationale for stepping up UK home production of Factor VIII (and other blood products) was thus one of cost, not of safety.

The cost-reduction argument was later supported by two Scottish studies, published in the British Medical Journal in 1976. A group from Glasgow, arguing for changes to allow more home treatment of haemophiliacs, mentioned among factors that might reduce the cost of home treatment: '... most of the freeze-dried concentrate used in the United Kingdom is imported and it is forecast that supplies produced in this country will be cheaper'.[39] An Edinburgh report pointed out the paradox of failing to invest in home production of blood

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Cryoprecipitate Method of Preparing AHF Concentrates, British Journal of Haematology, 27 (1974), 391-405. Rosemary Biggs, Director of Oxford Haemophilia Centre, chaired the Working Party: Maycock and Cleghorn were members.

[38] Ibid, 404.

[39] F. Carter, C. D. Forbes et al, 'Cost of management of patients with haemophilia', British Medical Journal, 1976 (2), 467.

products: 'Unless the blood transfusion services receive increased amounts of money and reappraise their functions and operation, it seems likely that they will have to rely increasingly on commercial (and costly) sources for the major plasma fractions.'[40] The problem can be characterized as one of tension between central investment versus regional current expenditures - as well as a lack of political will to reorganize the system, to ensure adequate supplies of plasma reached the centre from the regions. To 'reappraise their functions and operation' proved more feasible in Scotland, with its more centralized blood transfusion service, than in England and Wales where each regional BTC was semi-autonomous. Through the late 1970s, while Scotland headed towards self-sufficiency in blood products,[41] imported blood products occupied an increasing share of the increasing amount of Factor VIII administered south of the border.

Rising imports of commercial Factor VIII and a promise of self-sufficiency

Cost was only one of several possible considerations determining policy on blood products. The purity and safety of the product was another, hypothetically perhaps worthy of a good deal of expenditure. There were debates in the 1970s, and thereafter into the AIDS era of the 1980s, over the degree

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[40] J. D. Cash and M. Spencely, 'Haemophilia A and the blood transfusion service: a Scottish study', British Medical Journal, 1976 (2), 682.

[41] See: Cash and Spencely, 'Haemophilia A', for view that Scotland was virtually self-sufficient by 1980/81.

to which the use of paid donors increased the likelihood of hepatitis transmission. For example, an international haemophilia symposium held in Glasgow in 1980 discussed data on hepatitis, among other problems.[42] An increase in the incidence of both B and non-A, non-B hepatitis had been noted in 1974 and 1975, following the use of imported commercial freeze-dried Factor VIII from Europe and the US, to make up for the shortfall in NHS supplies. Other commercial concentrates were licensed for UK use in 1976; by 1980, six brands were in use altogether, of which four were made in the US from large pools of plasma obtained by plasmapheresis from paid donors, one was made in Austria, and the sixth was NHS Factor VIII, made using large pools of plasma from volunteer donors. Craske, virologist at the PHLS laboratory at the Withington Hospital, Manchester, responsible for this survey, was reluctant to commit himself on the question of whether the NHS product was less likely to transmit hepatitis than the commercial products, emphasizing the large pool size in the NHS process.[43]

In America, where commercial products were more widely used, the transmission of hepatitis B to haemophiliacs was clearly enormous. According to a 1983 report:

> Approximately 85% of all patients with clinically severe

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[42] J. Craske/ Public Health Laboratory, Withington Hospital Manchester, 'The epidemiology of factor VIII and IX associated hepatitis in the UK', in C. D. Forbes and G. D. O. Lowe (eds), Unresolved problems in haemophilia (Lancaster: MTP Press, 1980), pp. 5-14; and pp. 14-17, discussion of paper.

[43] The safety advantage of voluntary donations for whole blood was much clearer: Craske, 'Epidemiology of factor VIII and IX associated hepatitis', p. 6.

> haemophilia needing frequent transfusions with concentrates of Factor VIII or IX have serologic evidence of previous exposure to hepatitis B antigen (HBsAg), and up to 10% will be HBsAg carriers. The incidence of liver dysfunction is high, and liver biopsies from patients with haemophilia have shown a spectrum of liver diseases, from mild focal inflammation to chronic active hepatitis, cirrhosis, and even hepatic malignancies.[44]

In England and Wales, as the use of imported commercial clotting factors increased, incidence and levels of hepatitis-associated morbidity among haemophiliacs undoubtedly increased, though hepatitis was seldom recorded directly as the cause of death. Hepatitis was responsible for only two of the total of 89 deaths among patients with haemophilia A and 18 with haemophilia B during the period 1976-80.[45]

Overall, between 1968 and 1988 the consumption of Factor VIII in the UK increased ten-fold; between 1971 and 1980, the proportion of the demand met by imported commercial Factor VIII increased from zero to over 60 per cent. The rise in hepatitis among haemophiliacs at the same time as the rise in imported products does not prove a causal link - the NHS product could have been equally, or more, responsible - but there was a strong suspicion that imported Factor VIII carried a greater hepatitis hazard.[46]

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[44] G. C. White and H. R. Lesesne, 'Hemophilia, hepatitis and the acquired immunodeficiency syndrome', Annals of Internal Medicine, 98 (1983), 403.

[45] C. R. Rizza and R. Spooner, 'Treatment of haemophilia and related disorders in Britain and Northern Ireland during 1976-80: report on behalf of the directors of haemophilia centres in the United Kingdom', British Medical Journal, 286 (1983), 929-33.

[46] This view could have been partly due to the influence of Titmuss, as my colleague Virginia Berridge has pointed out.

The whole issue of trade in blood and blood products was becoming more and more highly politicized. A Granada television 'World in Action' two-part programme in 1975 brought the trade in blood and plasma to public attention, and spotlighted the increased hepatitis risk from imported blood products.[47] Directors of UK haemophilia centres made representations to government, and in 1976 Dr David Owen as Secretary of State for Health announced at the third European Regional Congress of the World Federation of Haemophilia, held in London, that the central Blood Products Laboratory would be upgraded with the aim of achieving self-sufficiency in UK production of Factor VIII by mid-1977.[48] However, despite embarrassment caused to successive government by concern over imported blood products, the upgrading of BPL was repeatedly delayed; first under a Labour government and then after 1979 under a Conservative government.

As well as pressure from the haemophilia lobby, there was pressure on the government from health unions, especially over the sale of whole blood collected within the NHS to overseas purchasers. Equally worrying were moves to sell blood to private companies in the UK. The union which represented most blood laboratory technicians responded angrily when it got wind of moves to open up the market in British blood, under the first Thatcher Conservative government:

> ... ASTMS would be totally opposed to any involvement of

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[47] 'Blood money', Granada TV, 1975: I am grateful to Professor A. J. Zuckerman, who acted as adviser for the programmes, for alerting me to this production.

[48] P. Jones, Personal record (see n. 58, below)

> private drug companies in blood products manufacturing in the UK. The raw material having been donated voluntarily and freely by the population, it was immoral to involve commercial enterprises in the utilisation of that raw material for profit.[49]

This tersely worded response to the threat of private enterprise in blood product manufacture in the UK offers an absolute moral stance, rather than an assessment of relative safety of commercial versus voluntary products. The union was probably correct to assume that donors who gave their blood free of charge would prefer it not to be bought and sold. It is quite refreshing to have this moral position iterated, independently of considerations of cost and safety.

Meanwhile the delays in implementing the plan to upgrade the Blood Products Laboratory continued. The will to allocate the necessary capital sum - which kept increasing the longer the scheme was delayed - was lacking, while the DHSS continued to displace responsibility for purchasing policy onto regional BTCs and haemophilia centres. According to one account, the plan for a new BPL was suspended almost as soon as it had been aired, in the first round of NHS cuts following intervention by the International Monetary Fund;[50] the irony was, the calculations which prompted the Chancellor to seek assistance were based on faulty Treasury forecasts.[51]

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[49] D. O. G. Craig, 'Blood products - the battle against private enterprise goes on', Medical World, 119, 9/10 (Sept/Oct 1981), p. 15.

[50] Bateman, 'Good bleed guide', 131.

[51] D. Healey, The time of my life (London: Michael Joseph, 1989), p. 381: 'If I had been given accurate forecasts in 1976 I would never have needed to go to the IMF at all' - budgetary requirement estimate for 1976 was £2,000 billion too high.

The problem of rebuilding BPL was not only one of costs but also of organization, with the need to ensure that adequate supplies of plasma flowed from the regional BTCs. Very little was done to increase this flow, right through to the 1980s.[52] There was also a question over who should run the Blood Products Laboratory. Until 1978, the MRC and the Lister Institute were jointly responsible for BPL.[53] When the Lister Institute was closing down in 1978, the North West Thames Regional Health Authority agreed to take over management of BPL for six months, since it fell within its area. In the event, North West Thames Regional Health Authority ran BPL for four years while the government decided (or failed to decide) what to do about it: whether to operate it as a separate health authority, as part of an existing health authority, as a trust or as a commercial concern.

The advent of AIDS changed the picture dramatically. Panic about the possibility that AIDS might be transmitted in blood and blood products threatened to impede the functioning of the blood transfusion service: donors showed reluctance to come forward, while patients were clearly alarmed about possible

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[52] J. Cash, 'The blood transfusion service and the National Health Service', British Medical Journal, 295 (1987), 617-9; but see also: E. L. Harris, Chair of Advisory Committee on the National Blood Transfusion Service, 'The blood transfusion service and the National Health Service', (Corr.), British Medical Journal, 295 (1987), 722-3, for claim that his committee set targets for plasma production from the regions to ensure full self-sufficiency of the new BPL in 1988.

[53] The Lister Institute had been set up in 1891, by voluntary effort, as a bacteriological research institute parallel with the Pasteur Institute in Paris and the Koch Institute in Berlin. See: H. Chick, M. Hume and M. Macfarlane, War on disease. A history of the Lister Institute (London: Andre Deutsch/ The Lister Institute, 1971)

contamination of transfused blood. In September 1983, following consultation with directors of regional BTCs, the DHSS produced a leaflet on AIDS and blood donors. Kenneth Clarke, then Minister of Health, announcing the leaflet's publication, said: 'It has been suggested that AIDS may be transmitted in blood or blood products. There is no conclusive proof that this is so.'[54] However, the fear was recognized and, since no test was yet available, the leaflet asked that anyone who thought they might have AIDS should refrain from giving blood.

This was scarcely the stuff to quell all qualms; nor did further information supplied to the press inspire great confidence. Massaging the figures a little, the DHSS claimed that: 'Half the Factor VIII used for the treatment of haemophilia in this country is produced here and the remainder imported from the USA'. Realising that the latter source was suspect, they added that the US Food and Drug Administration had laid down requirements intended 'to exclude donors from high risk groups from plasma donation' - presumably (though they did not spell it out) donors considered at high risk from AIDS, such as gay men and IVDUs. Implicitly admitting that US imports were recognized as hazardous, the press release offered a commitment already seven years old at the time of this 1983 press release:

> The Government is committed to making Britain self-sufficient in blood products - the National Blood Transfusion Service already meets the demand for whole blood - and is redeveloping the Blood Products Laboratory

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[54] DHSS Press Release: 'AIDS - and blood donation', 1 Sept 1983.

at Elstree over the next 3 years.[55]

The timescale was a little overoptimistic: it was another four years before the upgraded BPL was opened in 1987, and full functioning was not attained until mid 1988.[56]

The debate over infection of UK haemophiliacs with AIDS

The debate over liability for infection of many of the 5,000 or so haemophiliacs in the UK with the AIDS virus is analysed in detail elsewhere.[57] Peter Jones, Director of the Northern Regional Haemophilia Centre at Newcastle, who has been extremely active in the National Haemophilia Foundation, has given an insider's account, setting out the debates over treatment and dates at which shifts in understanding or policy took place.[58] Critical debates, in retrospect, centre on the timing of the introduction of two innovations: testing of individual donations - delayed in this country from March to October 1985 while a British test was developed - and heat treatment of Factor VIII concentrate. Each of these measures might help to render the product safer with regard to HIV (though not hepatitis) and it has been argued that there was a

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[55] Ibid.

[56] The foundation stone was laid by Norman Fowler, then Secretary of State for Health, in March 1984, and the new building was opened by the Duchess of Gloucester on 29 April 1987; the name was changed to 'Bio' (as opposed to 'Blood') Products Laboratory c. 1990. Thanks to staff at BPL for this information.

[57] Berridge, History of the present.

[58] I am extremely grateful to Dr Jones for permission to read and use this confidential account, and to my colleagues Virginia Berridge and Janet Foster for drawing it to my attention.

culpable delay which resulted in the infection of many more haemophiliacs with HIV than might otherwise have been the case.

The products which were safe for HIV could still transmit hepatitis; indeed the recommended switch from cryoprecipitate (used as an interim alternative to the more heavily infected concentrate) to heat-treated concentrate might increase transmission of non-A, non-B hepatitis. Towards the end of 1985, when the switch was recommended, although there had been AIDS deaths among haemophiliacs and alarm was growing, it was still not clear how much greater the AIDS threat was than that of hepatitis, which caused few deaths but considerable long-term liver damage among severely affected haemophiliacs.

The other strand of argument, connected with the thread running through this chapter, concerns the origins of plasma products. On the one hand we have Jones' view, tentatively expressed in 1983, that the pool size of NHS concentrate had increased to the point (over 3,500) where the benefits of using only voluntary donors might have been lost.[59] It was on this basis that, having had a haemophilia patient die of AIDS in November 1984, and in view of accumulating evidence on the value of heat treatment, Jones in December 1984 switched all his patients from NHS concentrates, which were not yet heat-treated, to commercial heat-treated concentrates.[60]

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[59] P. Jones, 'Acquired immunodeficiency syndrome, hepatitis and haemophilia', British Medical Journal, 283 (1983), 1737-8.

[60] P. Jones, Personal record, letter to colleagues explaining decision, 13 Dec 1984.

On the other hand, in spite of his patients having apparently been infected with AIDS by NHS blood products, Jones still believes that self-sufficiency in blood products in the 1970s could have prevented many British AIDS deaths. Jones notes that US companies were obtaining and processing plasma in African countries and Mexico, where American rules did not apply, then taking them through their US plants for re-export to Europe. The import and license controls in the UK, he suggests, were inadequate: the Chief Medical Officer of Health had no knowledge of the use of extra-US plasma sources by US companies.[61] Of course with AIDS, as with hepatitis, high endemicity could be as much a feature of some US source groups as of African populations; Jones' point is that the British authorities were ignorant of the perils they were allowing into the country. Yet the importation of plasma from developing countries was common knowledge in the haemophilia community in the early 1970s.[62]

Conclusions

In presenting the post-1970 history of hepatitis in the blood supply, this chapter has shown the introduction of testing to be something of a watershed for safety in whole blood transfusion, but not in the use of blood products. Testing all blood donations was a massive operation in terms of organization, and imposed extra costs on the transfusion

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[61] Jones, Personal record, pp. 70-1.

[62] Ibid, p. 72, referring to Bulletin 9 of the World Federation of Haemophilia and papers of 10th Congress 1975.

services; rapid, universal uptake cannot be assumed to be the inevitable course. Again, as with the application of testing in the renal unit outbreaks, we see a balance between local initiative and central co-ordination. One example was the North London Blood Transfusion Centre decision that testing for antibody and excluding those found to carry it was unnecessary; although the central advisory group did not follow this policy at first, it later prevailed. There is another parallel with the renal unit situation (where the PHLS played a crucial role) in the importance of certain allied structures: the central Blood Products Laboratory as a reference centre and producer of tests, and the regional blood transfusion centres in implementing as well as creating policy.

In describing and analysing the very different history of hepatitis in blood products, I have chosen to emphasize the failure to upgrade the Blood Products Laboratory to allow England and Wales to achieve the self-sufficiency in blood products which Scotland prided itself on by 1980. Use of imported factor VIII was partly explained for the 1970s in terms of factors other than safety, but insufficiency of the home supply meant that imports were bound to increase. Not only were the origins of commercial products suspect, so too was their regulation. But the debate over culpability for the infection of haemophiliacs with HIV/AIDS is complicated, and some interpretations would place more emphasis on delays in testing and in using heat-treated products, arguing that the wish to use British tests and products militated against the

best interests of haemophiliacs. The case of French haemophiliacs infected with HIV, due to a lengthy delay in the introduction of testing, would seem to support this view.

A recent German scare over HIV in the blood supply gives a rather different slant. Here, testing was farmed out to private companies by a government tranfusion service that could not cope with the task alone. Two of these firms were found to have skimped on testing procedures to maximise profits - a totally unethical practice which led to infection and deaths among recipients of blood transfusions. These firms seem also to have bought blood from donors who would not be accepted in a voluntary system.[63] Here, the Titmuss theory seems to have been borne out, and paying for blood yet again led to disaster, as the profit motive supplanted altruism. If we look at blood donation as an instance of organ donation, this message is further reinforced.

Ruth Richardson has argued in relation to the supply of bodies for anatomical dissection in the nineteenth century, and the supply of organs for transplantation in the twentieth century, that payment by recipients or intermediaries invariably tends to produce malpractice in procurement: grave robbing and murder in the supply of corpses; exploitation, coercion and murder in the case of organs.[64] Blood, as a replaceable

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[63] 'When fear flows like blood', report by Steve Crawshaw, The Independent, 18 Nov 1993, p. 23.

[64] R. Richardson, 'Spurning the gift, presuming upon consent or bargain & sale - which path for transplantation?', talk for 'Doctors and the state' seminar, Wellcome Institute for the History of Medicine, London, 20 Oct 1993.

tissue, may not call forth such extremes, but its extraction as a market commodity from the poor and desperate, whether in underdeveloped or developed countries, clearly tends to involve exploitative relationships. If the line of argument followed in this chapter is correct even in part, then blood impurely obtained has wreaked a terrible revenge, carrying hepatitis and AIDS in preventable channels.

CHAPTER 6: HEPATITIS RESEARCH IN THE 1970S, INFORMAL NETWORKS, AND EXPERT COMMITTEES [1970-1980s]

The discovery of the Australia antigen, and the recognition of the virus and core particle of hepatitis B by electron microscopy, described in Chapter 3, opened up enormous new possibilities for research on the disease. Turning to policy, Chapters 4 and 5 centred on renal dialysis units, and the blood supply, two areas where hepatitis B figured prominently around 1970. Policies in the renal unit and blood arenas aimed at solutions using a combination of testing and raised standards of hygiene: the latter alone were stressed for most health care workers, as Chapter 7 will show. While there appeared to be no further notable outbreaks of hepatitis B after the early 1970s, the unknown carrier population posed a lingering public health hazard both within the health care setting and for the general population.

How far did the concerns of policy makers set an agenda for research in hepatitis B after 1970?[1] Rather than follow public health concerns, hepatitis research seems often to have been shaped by the agenda of the clinical and academic settings in which it was located. The first section of this chapter traces the outlines of burgeoning hepatitis research in the 1970s: as with any topic, there were different levels of research. The main areas of 'applied' research were test development and vaccine research; there was very little on the

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[1] In the 'rational' model of the relation between research and policy discussed in Chapter 1 above, policy questions call for research to provide a logical basis for policy decisions.

carrier state and how best to manage it. Most hepatitis research, while not necessarily 'pure', was directed towards scientific questions, at one or two removes from policy - although, as in the case of wide ranging epidemiological studies, such research could carry policy implications. Using the newly available test, many researchers examined the mode of transmission of the virus, and how widespread it was within populations and sub-groups. Others studied its behaviour in the human body - the 'natural history' of the virus and the disease it caused - including the complexities of the immune response. Certain difficult undertakings, particularly tissue culture, a staple of virological research, consumed much effort but produced mainly negative findings. A review of the range of research will be given in the first part of this chapter.

How research gets done used to be something of a mystery, inadequately illuminated by personal accounts; but for the past two decades a growing analytical literature on the sociology of laboratory work and the construction of scientific 'facts' has built up a more complex and convincing picture.[2] Prompted partly by this literature, partly by themes which emerged from a number of interviews, a more anthropological approach will be used in the middle section of this chapter, to trace a particular aspect of the research process: that is, networks of exchange between groups of

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[2] For useful reviews, see: Lowy, 'Recent historiography of biomedical research'; and M. Nicolson, 'Heterogeneity, emergence and resistance: recent work in the sociology of laboratory science', in G. Lawrence (ed.), Technologies of modern medicine (London, Science Museum, 1994), pp. 111-19.

researchers in London, here interpreted as an informal means of co-ordination of research. This section looks at different styles of research and researchers: sites of research, types of technical skills employed, and exchanges between them. Of special interest for the next section is the growth of expertise and the emergence of recognised experts in the field.

A third section looks at more official coordination, chiefly MRC backing for research in this field through the 1970s and into the 1980s. Individual project funding by the MRC can be seen as one facet of policy on scientific medical research, while sub-committees dealing with aspects of hepatitis B are another. This is the location where we might expect the interface between research and policy to emerge most visibly, as occurred during the war when the MRC Jaundice Committee bracketed the Ministry of Health, MRC and armed forces in forming research policy. Yet another strand of committees has been more directly involved in recent health policy-making: that is, advisory groups to the Department of Health. These too have close links with research, since their composition has closely mirrored the MRC committees. Although it is difficult to find out what happens in confidential advisory groups, it is worth asking about the selection and role of 'experts'. How far do they conform to the model of the type of scientific researcher favoured by the MRC? Or perhaps such semi-secret groups reflect the informal networks discussed here, and also include 'outsiders' who have achieved a reputation for expertise. Certainly we should weigh up the

part played by informal as well as formal structures in shaping experts, who then form a link between medical research and policy making. Finally, although again it has been difficult to find evidence for this, there is the perhaps pre-eminent role of medical civil servants who filter the advice received from experts, and finally decide policy.

Configurations of hepatitis research in the 1970s

The availability of the antigen test stimulated a wide variety of studies of hepatitis B during the 1970s. Investigators no longer needed close clinical study of patients - for many purposes it was sufficient to estimate the presence of antigen or antibodies in serum. The immunodiffusion test was simple and cheap, within the capacity of third world laboratories as well as the main medical centres. The largest category of published work was epidemiological, using the antigen test on serum from groups or populations to find rates of hepatitis B and suggest routes of spread. Hundreds of clinicians with access to cases of hepatitis added to the literature, rapidly dispelling the idea that this was a disease of needles and syringes only.

Many epidemiological studies were carried out by authors who only published once or twice on hepatitis B. These were oriented towards clarifying routes of transmission: needles and blood were frequently invoked, but in a wide range of situations. Besides post-transfusion hepatitis and intravenous drug use, there were detailed studies of antigen

rates among health workers; and associated with tattooing, ear-piercing, and acupuncture.[3] Following the observation that hepatitis B tended to spread among members of the same household or within mental institutions,[4] there was interest in whether the antigen could be found in body fluids other than blood, especially saliva.[5] Allied to this were studies indicating sexual spread of the disease - both among homosexuals and heterosexuals.[6] Another concern was the possibility of insect transmission, as a tentative explanation for the much higher rate of the disease in warmer climate countries.[7]

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[3] For example: N. A. G. Mowat et al, 'Outbreak of serum hepatitis associated with tatooing', Lancet, 1973 (i), 33-4; E. H. Boxall, 'Acupuncture hepatitis in the West Midlands, 1977', Journal of Medical Virology, 2 (1978), 377-9. Studies of occupational hazard were legion; surgeons and dentists attracted perhaps most attention. Patients were studied in settings where hepatitis was a known hazard (renal units, MHIs) but for an unusual study of patients in Ireland, see: G. R. Fitzgerald et al, 'Hepatitis-associated-antigen-positive hepatitis in a tuberculosis unit', Gut, 16 (1975), 421-8.

[4] This began with the MRC wartime study, and was expanded by the Willowbrook study described in Chapter 2.

[5] R. Ward et al, 'Hepatitis B antigen in saliva and mouth washings', Lancet, 1972 (ii), 726-7. The query over the role of saliva in hepatitis B transmission was unresolved by the late 1970s, causing heated debate in New York court cases over infected carriers in schools; see: Muraskin, 'Controversy over integration of retarded hepatitis B carriers', esp. pp. 85-8.

[6] K. W. M. Fulford, D. S. Dane et al, 'Australia antigen and antibody among patients attending a clinic for sexually transmitted diseases', Lancet, 1973 (i), 1470-3; J. Heathcote, C. H. Cameron and D. S. Dane, 'Hepatitis-B antigen in saliva and semen', Lancet, 1974 (i), 71-3; W. Szmuness et al, 'On the role of sexual behaviour in the spread of hepatitis B infection', Annals of Internal Medicine, 83 (1975), 489-95.

[7] Two contrasting methodologies appear in: A. M. Prince et al, 'Hepatitis B antigen in wild-caught mosquitoes in Africa', Lancet, 1972 (ii), 247-50; and a study on laboratory-bred insects: N. A. Byrom et al, 'Role of mosquitoes in transmission of hepatitis B antigen', Journal of Infectious Diseases, 128 (1973), 259-60.

The outbreaks of hepatitis B in renal units, which might have been expected to generate an enormous research interest, were subjected to only moderate epidemiological scrutiny, possibly because they were often reported in unpublished form.[8] Prevalence in renal unit patients and staff, and possible routes of transmission, were reported. Some studies were speculative, for instance the antigen was injected into laboratory cockroaches; others were empirical, for example one which found the antigen in situ on stainless steel surfaces but not on textiles.[9] British studies looked not only at prevalence but also at means of prevention, and were linked to the Rosenheim enquiry. By the mid-1970s the UK Public Health Laboratory Service was able to report that hepatitis B was on the retreat in kidney units.[10] No 'harder' science than the immunodiffusion test had been required to achieve this result.

One set of epidemiological studies looked at the varying prevalence of markers of hepatitis B in different populations around the world; these studies had begun with Blumberg's NIH team almost before the Australia antigen-hepatitis B link was established.[11] They found a relatively low prevalence of

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[8] The Rosenheim Report has information on unpublished as well as published outbreaks.

[9] H. Zebe, R. Sanwald and E. Ritz, 'Insect vectors in serum hepatitis' (Corr.), Lancet, 1972 (i), 1117-8; M. Favero et al, 'Hepatitis-B antigen on environmental surfaces', Lancet, 1973 (ii), 1455.

[10] S. Polakoff, 'Hepatitis B in retreat from dialysis units in United Kingdom in 1973', British Medical Journal, 1976 (1), 1579-81.

[11] See Chapter 3, section on Blumberg.

Australia antigen in North American and European populations (under one per cent) and a much higher rate (over five per cent) in Africa and Asia.[12] Mother to child transmission at or soon after birth accounted for early acquisition of the disease and a higher chance of developing carrier status in high prevalence countries.[13] Hepatitis B carrier status was linked with primary liver cancer, a form of cancer rare in wealthy countries but common in poor countries with a high prevalence of hepatitis B.[14] This link would have complex policy implications once a vaccine became available. The saving of life in relation to chronic diseases, particularly liver cancer, would be far greater than for hepatitis B alone, but the long-term effects required careful analysis if overstretched health care systems in Africa and Asia were to fund mass vaccination.[15]

Much research, especially in the UK, focussed on developing more sensitive tests, with the aim of reducing false negatives. There was a commercial incentive since the most successful tests would sell in enormous numbers for blood donation testing. Research and development of tests in

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[12] A. M. Prince, 'Prevalence of serum-hepatitis-related antigen (SH) in different geographic regions', American Journal of Tropical Medicine and Hygiene, 19 (1970), 872-9.

[13] But in some areas, especially Africa, environmental transmission during infancy seems more important.

[14] A useful overview is provided in: London and Blumberg, 'Comments on role of epidemiology in investigation of hepatitis B'.

[15] A. Hall et al (The Gambia Hepatitis Study Group), 'The Gambia hepatitis intervention study', Cancer Research, 47 (1987), 5782-7.

pharmaceutical company laboratories, often in collaboration with health service or university laboratories, exemplifies the science/industry interface.[16] Despite the size and expense of electron microscopes, some tests used EM techniques for diagnosis by direct visualization of infective particles. However, most tests built on the principle of immune reactions utilized in the early tests, improving on sensitivity through the introduction of electricity (immuno-electrophoresis) or radioactive isotopes (radioimmunoassay).[17] All tests required prior separation of material by more or less rigorous fractionation and centrifugation. There was initially no standardisation; laboratories freely developed and used their own tests, meeting varied requirements as to sensitivity versus ease and speed of preparation, depending on the amount of samples they had to process. A public health laboratory would test only a handful of samples for hepatitis B in a year (although many samples being tested for other diseases might actually carry hepatitis B), whereas a blood transfusion centre had to test every donation and therefore required mass processing methods.

Evaluation of commercially produced tests and comparison

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[16] For example, the Wellcome Foundation's Ian Cayzer under the direction of John Beale developed 'Hepatest' in conjunction with workers at the Middlesex Hospital, London, using sera from the North London Blood Transfusion Centre; see: I. Cayzer, D. S. Dane et al, 'A rapid haemagglutination test for hepatitis-B antigen', Lancet, 1974 (i), 947-9.

[17] Radioimmunoassay, for example the commercial 'Ausria' test, was regarded as much more sensitive than counterimmunoelectrophoresis; see: H. J. Alter, P. V. Holland et al, 'The Ausria test: critical evaluation of sensitivity and specificity', Blood, 42 (1973), 947-57.

between efficiency in using tests was undertaken by some research laboratories. A 1974 study compared the proficiency of 40 blood screening laboratories in different countries, using the same test (counterimmunoelectrophoresis), and found only two succeeded in matching the results set by reference laboratories. With low titre samples (containing little antigen), proficiency ranged from 15 to 85 per cent.[18]

Other research fell within the disciplinary boundaries of immunology, virology and hepatology. Much of the work depended heavily on antigen and antibody testing, combined with standard immunological techniques and liver function tests, to study variations in immune responses and liver pathology, establishing the natural history of the disease in both its acute and chronic form.[19] Advances in understanding depended on the new-found ability to detect antigen at different stages in the development of the illness, linking fluctuations in antigen and antibody levels with clinical manifestations. At least three antigens were identified: the surface, core and 'e' antigens.[20] The antigens themselves were subjected to biochemical processes of purification and analysis, as was the whole virus or 'Dane particle'.

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[18] B. P. L. Moore, D. Meade et al, 'An international proficiency survey for the detection of hepatitis B antigen and antibody in blood donations by counterimmunoelectrophoresis', Vox sanguinis, 26 (1974), 128-32.

[19] See for example, from King's Liver Unit: A. L. Eddleston and R. Williams, 'Inadequate antibody response to HBsAg or suppressor T-cell defect in the development of active chronic hepatitis', Lancet, 1974 (ii), 1543-5.

[20] See Purcell, 'Hepatitis B' for review: identification of 'e' as a marker of high infectivity was a prolonged process.

As well as providing clinical material for studies in pathology, immunology and virology - yielding blood, serum and tissue samples for analysis in laboratories - patients with hepatitis B were also the location for treatment which, at this stage, was experimental. There was some indication of success with interferon, although progress was tentative and side-effects could be unpleasant.[21] Prevention by active or passive immunization offered more promise.[22] Immediate passive vaccination showed some evidence of obviating the worst impact of needlestick injuries where there was a known risk of hepatitis B infection.[23] Active vaccination, while offering no direct succour to patients with hepatitis B, would (when introduced) protect the close contacts of carriers, allowing them to live more normal lives.[24] But hepatitis remained through the 1970s a potentially lethal disease for which there was no prevention and no cure.

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[21] Group B (a self-help group of gay men with chronic hepatitis), interview, 12 May 1991.

[22] Active vaccination: a vaccine (with antigenic material) stimulates the body's immune system to produce antibodies, giving longterm protection, e.g. smallpox vaccination, measles immunization. Passive immunization: a serum fraction containing antibodies is given to combat infection in the short term; this may be general, e.g. gamma globulin, or specific, e.g. hepatitis B specific immunoglobulin, prepared from serum of donors with antibodies to hepatitis B.

[23] J. E. Maynard, 'Passive immunization against hepatitis B: a review of recent studies and comment on current aspects of control', American Journal of Epidemiology, 107 (1978), 77-86.

[24] This is apart from its obvious and enormous public health potential. Active vaccine was first approved in US after trial among New York gay men; see: W. Szmuness et al, 'Hepatitis B vaccine: demonstration of efficacy in a controlled clinical trial in a high-risk population in the United States', New England Journal of Medicine, 303 (1980), 833-41.

London networks of hepatitis B investigations in the 1970s

So far, the broad outlines of hepatitis B research in the 1970s have been sketched: this section will look more closely at several London workers involved in hepatitis B research - a mixture of clinicians and scientists, from different specialities and types of institutions. Sites where research took place in this period either had close connections with sources of clinical material, as in virology departments of teaching hospitals, blood transfusion centres, reference centres and the Blood Products Laboratory, or else they secured links with such sources, as in the case of pharmaceutical companies. Many of those engaged in research also had practical functions to perform - often, checking samples for presence of antigen, either to give opinions on particular patients, or to ensure that blood and blood products were free of hepatitis B. On the other hand, there were scientists who received material from clinicians and worked exclusively in a research capacity.

Let us take first of all a technique that appears prominently in hepatitis B research: electron microscopy (EM), the preserve of technical specialists in a variety of bio-medical specialties and institutions, which entered virology in the late 1950s when negative staining revolutionised the scale of micro-organisms that could be seen, bringing viruses within view. More than one investigator thought of applying this technique to hepatitis, since the difficulties of tissue culture closed off more established avenues of access to the

virus. We have seen (in Chapter 3) how David Dane, clinician and virologist at the Middlesex Hospital in London, successfully used EM in 1969, together with colleagues Colin Cameron and Moya Briggs. They were the first to identify the virus, which became known for some time afterwards as the 'Dane particle'.[25] In Dane's account the timing of this discovery was contingent on his department's acquisition of an electron microscope (funded by the Wellcome Trust), and also on his professor's unrelated request that he check a blood sample using the new Australia antigen test. Dane transcended the original request to conduct the test, and applied EM technique - with the aid of his colleagues, Cameron and Briggs. It was Dane, however, who was required to defend the finding, as controversy simmered over the nature of the Dane particle and whether it could indeed be regarded as the virus.

Dane's case was, in part, establised by the work of another worker with greater EM technical expertise, June Almeida, also discussed above (in Chapter 3). Almeida's moves from Toronto, to London, with Waterson - first at St Thomas's and then the Hammersmith - were accompanied by a further breakthrough in the scale of visibility, with the technique known as immune electroscopy, allowing antigen particles to be seen. Contact with Zuckerman launched Almeida on an EM investigation of the antigen-virus complexes and viral structure of hepatitis B. In 1970, she revealed the core of the Dane particle, enhancing

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[25] The relative roles played by each member of the team cannot be verified either from the oral record or later published accounts, but see: D. S. Dane, 'Discovering the virus of hepatitis B', Transfusion Microbiology Newsletter, 11 (1991), 16.

the case for identifying the particle as the hepatitis B virus and opening avenues for further research. Soon after this, Almeida left the Hammersmith to join the Wellcome Foundation laboratories at Beckenham; her EM expertise was eminently transferrable.[26]

The crossover between the public sector and industry noted in Almeida's career appears again in the case of John Beale, a clinician who one might say was remoulded as a scientist, with microbiological rather than EM expertise. After working on tuberculosis in the Royal Air Force and on influenza in a public health laboratory, Beale moved to Toronto in the early 1950s. This was just before the change that made electron microscopy an exciting tool for virology. Beale learned tissue culture methods, and helped produce the Salk polio vaccine on a large scale. Back in the UK, he joined the pharmaceutical company Glaxo, where he became head of vaccine production when the previous head - who had also been at Toronto - resigned, following the discovery of live polio in the killed vaccine.[27] Looking for someone to test the polio vaccine further, Beale contacted Dane, beginning a long and fruitful collaboration. In 1969, Beale moved to the Wellcome laboratories at Beckenham where his brief included diagnostic reagents as well as vaccines; thus he oversaw Australia antigen testing for Wellcome. Beale's contact with Dane

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[26] Interviews, J. Almeida, 29 January 1993 and J. Beale, 26 February 1993.

[27] Beale, interview. The finding was made in safety tests in the laboratory; there was no question of a threat to those receiving this vaccine, but the head of production felt obliged to resign.

possibly aided Wellcome's recruitment of Almeida.[28]

Zuckerman, the clinician and researcher who made hepatitis B his life's work, began his career like Beale with the Royal Air Force; he was seconded to Colindale in 1960 to work on viral hepatitis because of the continued outbreaks among service personnel.[29] The problem arose when syringes used for mass inoculations were inadequately sterilized - a finding already made during the war by the Jaundice Committee, but evidently needing to be rediscovered. As early as 1971 Zuckerman was recommending that drug clinics issue clean syringes to clients to reduce the spread of hepatitis B.[30] In a sense, even before the Australia antigen discovery, Zuckerman had become a hepatitis B expert, a position on which he ably capitalised. His greatest skills appear to have been those of co-ordination; he sat on most of the UK and international committees, read everything published on hepatitis B, and became the central reference resource for

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[28] In 1972, soon after Almeida's arrival, Blumberg visited the Wellcome laboratories to promote his serum vaccine, which Beale and Almeida regarded it as scientifically weak. Other companies (Merck in the US) produced a serum-derived vaccine; Wellcome tried to develop an alternative vaccine, ultimately without success. In 1992 Wellcome closed their vaccine production division at Beckenham, largely due to the failure of their hepatitis B vaccine development: Beale, interview.

[29] A. J. Zuckerman, interview, 8 June 1992: his location was the Epidemiological Research Laboratory, Central Public Health Laboratory, Colindale, London. See: A. J. Zuckerman, 'The epidemiology of acute hepatitis in the Royal Air Force', British Journal of Preventive and Social Medicine, 18 (1964), 183-8.

[30] J. Hunter, M. Carella et al, 'The Australia (hepatitis-associated) antigen amongst heroin addicts attending a London addiction clinic', Journal of Hygiene of Cambridge, 69 (1971), 565-70; Zuckerman was a co-author.

WHO, based at LSHTM in London. Zuckerman offered a focal point through the reference centre at LSHTM, providing material and validation for many other researchers, all of whom were indebted to him to some degree. His co-ordinating role was both national and international.

Hepatitis B research in the LSHTM virology department was promoted by Zuckerman's recruitment of Colin Howard, a virologist who joined the department in 1971 after completing a master's degree in virology at Birmingham.[31] Howard brought scientific expertise, later demonstrated in his doctoral thesis on the biochemical structure and behaviour of the surface and core antigens of hepatitis B, as well as other work.[32] He collaborated with Zuckerman in hepatitis B projects, including an attempt to develop a 'micelle' vaccine as an alternative to Blumberg's serum based vaccine. Howard developed a second field of research interest, in the arenaviruses, but hepatitis B remained a major interest. Zuckerman also recruited another virologist, Kwesi Tsiquaye, to his team.[33] As we have seen, Zuckerman's access to scientific expertise was not confined by the walls of his laboratories in the LSHTM. He produced collaborative work with colleagues both locally, as in the case of Waterson and

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[31] Under a virologist called Peter Wildy from Glasgow - the rival centre to London; C. Howard, interview, 25 November 1992. The London-Glasgow rivalry was also important for AIDS.

[32] C. Howard, 'Studies on the nature of hepatitis B antigen', PhD thesis, University of London, 1976.

[33] Tsiquaye remains at LSHTM; Zuckerman left in 1989 to become Dean of Royal Free Hospital Medical School, London; Howard left in 1990 to become Professor of Microbiology and Parasitology at the Royal Veterinary College, London.

Almeida, and abroad, especially the US. His name appears on over nine hundred publications including standard texts on viral hepatitis.[34]

If the LSHTM reference centre was a node of research expertise, and one type of 'sample bank', there were others: the central Blood Products Laboratory (BPL), and certain blood transfusion centres. In the mid-1970s, Tom Cleghorn, head of North London Blood Transfusion Centre (NLBTC), recruited a scientifically trained virologist, John Barbara, with a view to utilising his expertise in research as well as service capacities. Transfusion screening for hepatitis B, as Barbara has pointed out, offered enormous scope for research: it could be viewed as the most massive microbiological sampling ever undertaken. Probably because their service role was dominant, and they had no research tradition, few blood transfusion centres capitalised on this golden research opportunity; NLBTC and Glasgow were leaders, and 'friendly rivals', in the enterprise.[35] Detection of different antigens in donors' blood enabled Barbara and colleagues to look at incubation and inapparent infection. Follow-up allowed them to discover at what point, if ever, donors who were carrying the 'e' antigen, a marker of high infectivity, seroconverted to 'e' antibody. They supervised the plasmapheresis of high-titre carriers - those with a high concentration of antigen in their blood - to produce the raw material Zuckerman and Howard needed for their 'micelle' vaccine project.

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[34] For example: Zuckerman and Howard, Hepatitis viruses of man.

[35] J. Barbara, interview, 13 July 1992.

So Barbara's expertise was used in a routine capacity in the transfusion service; in a research capacity to look at the natural history of the disease; and to provide specialist raw material for others' research and development. The serum used to develop Wellcome's Hepatest was provided by Cleghorn and Barbara of the NLBTC.[36] The NLBTC team also played a role in the standardisation of microbiological purity of material for transfusion; they provided plasma from one of their donors for the British, and later international, standard on hepatitis B surface antigen. This became the basic measure which defined whether any other sample was to be cleared for use, the 'Go/NoGo' quality control.[37] In developing his research roles, Barbara was able to build on longstanding contacts with Dane at the Middlesex Hospital and BPL at Elstree.

At BPL, Brian Combridge, a laboratory technician, worked under Sir William Maycock on blood products including specific immunoglobulin, and then from 1970 on successive hepatitis B tests.[38] He developed a radioimmunoassay in collaboration with Dane and Cameron at the Middlesex, and Barbara at NLBTC, which reputedly saved the National Health Service ten million pounds.[39] Combridge, who remained humbly at the same bench for forty years, received little acclaim for his work. He represents a type of technique - highly skilled assay work -

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[36] Beale, interview.

[37] Barbara, interview.

[38] B. Combridge, interview, 19 June 1991.

[39] D. S. Dane, personal communication, 19 Aug 1992; Dane had estimated the saving at £20m but revised this to £10m after consulting John Barbara.

at a type of sample bank - the BPL - which became a nodal point for exchanges with other workers despite this particular worker's relative immobility in terms of career and networking.

Which of the people whose careers have been outlined in this account, all of whom had some degree of technical expertise, emerged as 'experts'?[40] Two figures emerge as authorities consulted by central government and marked out by peer recognition: Zuckerman and Dane.[41] Zuckerman is probably more closely identified with hepatitis B than anyone else in the UK: he is also a leading international expert. Dane appears both as an expert authority and someone whose technical expertise was recognized by others, but less recognized in academic terms. His networks were extensive but far more local than Zuckerman's - with Cleghorn and Barbara at North London BTC, with Maycock and Combridge at BPL, with Beale and Cayzer at the Wellcome laboratories, with Polakoff and Vandervelde at the PHLS viral reference laboratory - all within striking distance of his base at the Middlesex. As an expert on the advisory committees that decided about screening policy, for example, Dane was probably influenced more by the consensus of colleagues with a public health orientation than

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[40] For a fuller discussion of types of expertise, see: Stanton, 'Blood brotherhood'.

[41] A clinician with research interests in hepatitis B, interviewed 11 Nov 1992, listed as the 'big four' of hepatitis B in Britain: Zuckerman, Roger Williams (Institute of Liver Studies, King's College Hospital), Howard Thomas (Professor of Medicine, St Mary's Hospital) and J. Banatvala (Professor of Virology, St Thomas's Hospital); another frequently cited authority is Dame Sheila Sherlock, lately of Royal Free Hospital. These are all London teaching hospitals.

by the latest ripple of excitement on the scientific hepatitis B front. Through his extensive networks of contacts, Dane facilitated interactions of other workers, including exchanges of materials.

The transfer of samples of blood or serum often appeared at significant points in people's accounts, as the 'liminal actions' that shifted them into hepatitis research (e.g. Almeida, Barbara, Combridge, Dane);[42] the supply of material was clearly important in continuing research. The often mentioned exchange of materials represents an informal form of co-ordination. The nature of the material leads to a notion of 'blood brotherhood' between investigators; a sort of tribal effort of altruistic scientists. The apparent generosity of sharing should not mislead us, since sharing samples of serum could establish indebtedness, of the recipient to the gift-giver.[43] The gift might be given to someone with special skills appropriate to a line of enquiry, which in a sense they then lend to the giver. In the case we are dealing with here, hepatitis B in the 1970s, clinicians could act as brokers, since they had unique access to the research material. They were nodal points, thus they become experts.[44] But they needed scientists or technicians with special expertise to manipulate the material they had gathered. To some extent it

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[42] See: J. Stanton, 'Hepatitis research and career trajectories', talk given to Health Matters Symposium, Science Museum London, 5 March 1993.

[43] Mauss, The gift.

[44] This would change with the development of animal models and genetic engineering, which enabled scientists to become more independent of clinicians.

was a symbiotic process.

Another element of 'blood brotherhood' emerged from some of the interviews. There were stories of carrying vials of blood in a briefcase on the tube, or receiving samples from abroad by post (not always in bubble-pack envelopes) - tales which seemed, perhaps subconsciously, intended to alarm the lay person conducting the interview. Such accounts speak of danger and excitement, but above all of the special quality of being an insider, one of a group of initiates. Those within the group are not all equal, and terrific strains existed between some of them, especially those vying for primacy. There was competition, too, between centres, as for example between London and Glasgow BTCs. But all shared a community of experience, in handling the danger of hepatitis B in infected blood and serum with confidence - and with science, another mysterious realm which excludes non-experts.

Official co-ordination: committees and the role of 'experts'

Official structures which co-ordinated information emerging from scientific and epidemiological research on hepatitis B appear to have followed a similar pattern at national and international levels. In Britain, the MRC set up a working party on hepatitis under its longstanding transfusion research committee, just as WHO discussed hepatitis in association with blood transfusion. According to Zuckerman, it was he who instigated the first MRC hepatitis committee in 1966, which is possible given that he was already conducting research in this

field by then. On the other hand, an MRC working party on post-transfusion hepatitis, with Zuckerman as secretary, first appears in the published record in 1970/71.[45] Clearly, this was closely allied with the Maycock advisory group on testing for Australia antigen, but the MRC group had a more general brief to oversee research.

In April 1971, a 'conference of experts' was called together jointly by the MRC and the DHSS to review hepatitis research with special reference to dialysis and transfusion, to feed into the Maycock and Rosenheim committees' deliberations.[46] In addition to collating existing research, the conference made recommendations regarding future lines of enquiry:

> they included the extension of epidemiological studies on Australia-antigen-positive subjects and their contacts, and further studies on the pathogenesis of serum hepatitis (with particular reference to the role of the immune response) and the possible prophylaxis of the disease in those at risk.[47]

How far were these research aims realised? As we have seen, a large proportion of research through the 1970s consisted of epidemiological studies, more often looking at prevalence in certain populations or groups rather than tracing contacts of antigen-positive individuals. The working of the disease within the body was also a subject of research, but much virological work was hampered by the difficulty of tissue

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[45] Medical Research Council, Annual Report for 1970/71, p. 112, under 'Blood Transfusion Research': Working Party on Post-transfusion Hepatitis with Dr W. d'A. Maycock as Chair and Dr A. J. Zuckerman as Secretary.

[46] Medical Research Council, Annual Report for 1971/72, p.24; the location of the conference and names of experts invited are not given.

[47] Ibid, p. 25.

culture. If 'prophylaxis' might be taken to mean vaccination, then that too was a central line of enquiry in the 1970s. But it is hard to trace a direct line from the conference quoted above, to these and many other branches of research into hepatitis B, conducted in a wide variety of NHS and academic settings; such research seems to have flourished under an impetus which was not largely generated by the MRC.

An area in which the MRC most speedily attempted to promote research involved prophylaxis with specific immunoglobulin, a different matter from vaccine development. This was based on earlier experience with specific serum, and with general immunoglobulin, for various diseases.[48] It was a project with a contentious background in the period of the first Maycock committee of 1970-72. When Dane suggested that blood with a high level of antibodies to hepatitis B might be used to make specific immunoglobulin (HBIG), the majority of committee members argued that both antigen and antibody-positive blood should be discarded, as potentially dangerous:

> Zuckerman and the other virologists on the Committee thought my suggestion was wrong and dangerous and they were dismissive of the whole idea. If they had accepted my explanation of the nature of Australia Antigen (HBsAg) and its relaton to the virus, which I had published shortly before, they might have been more sympathetic, but they did not.[49]

There was room for uncertainty, since some antibodies are not

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[48] See Chapter 3 for recognition of problems associated with pre-war measles convalescent serum and wartime use of mumps convalscent serum, both of which caused outbreaks of hepatitis; see also: MRC, Annual Report, 1972-73, p. 37.

[49] D. S. Dane, 'Hepatitis B immunoglobulin', personal account (typescript), encl. with letter to author, 30 Nov 1992, p. 2.

protective but only indicate the presence of the virus.[50] But clearly in the conflict between expert opinions, that of Dane who had the most intimate knowledge of the virus weighed less than that of more established virologists. It should be recalled that Dane together with Cleghorn of the NLBTC held a minority view on the safety of strongly antibody positive blood. While other centres were discarding such blood, Dane and Cleghorn were collecting the plasma with a view to getting a trial batch of HBIG made at the Blood Products Laboratory.

By the end of 1971, majority opinion had shifted in the light of further evidence from the US on the utility of specific immunoglobulin; and there was particular concern to provide some safety net for health workers involved in needle-stick accidents, which in settings such as renal units carried a high risk of infection with hepatitis B. The MRC committee was briefed to 'consider the feasibility of producing high-titre immunoglobulin that would be specific against Australia antigen and suitable for use in clinical trials'.[51] The chairman, Dr J. H. Humphrey, a well-known immunologist, wrote to ask Dane if he had any suggestions:

> I do not think he can have been told that until a few months before I was the isolated advocate and driving force behind the HBIG project! It was not for me to tell him. I can remember Dr MacCallum coming to see me on his way to the first meeting to be briefed on the subject. I was very conscious of being excluded.[52]

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[50] Currently the best-known example is HIV: the antibody is a marker for the presence of the virus but apparently affords no protection against AIDS.

[51] MRC, Annual Report, 1972/73, p. 37.

[52] Dane, 'Hepatitis B immunoglobulin', p. 3.

Excluded from the inner circle, Dane was nonetheless used as a supplier, for the next ten years according to his account, as the Middlesex/ North London BTC axis continued to test for antibody and persuade high-titre donors to give extra plasma by plasmapheresis.[53] Dane was disgruntled at being treated like 'a grocer' without encouragement or feedback, and years later he tried to find out the reason for his exclusion from the HBIG committee, but was told that 'no useful purpose would be served' by going into the matter.[54] For whatever reason, Dane apparently was not an 'MRC type' researcher.

Co-ordination of research was achieved by the MRC in general terms, not by organizing or funding multiple research programmes, but by surveying the whole field of research conducted on hepatitis B from time to time, and disseminating reviews of research through MRC annual reports. In some ways this operation closely reflects the functioning of WHO committees dealing with viral infections:[55] it is probable that Zuckerman, who sat on the WHO committees, was the author of the MRC contributions.[56] In addition to his research,

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[53] Most blood transfusion centres ceased testing for antibody once they were no longer required to discard antibody positive donations. In his account, Dane emphasised that the MRC committee and BPL did not ever stipulate how much plasma they wanted or what titre of antibody they considered suitable.

[54] Ibid, p. 4.

[55] Notably the WHO Expert Advisory Panel on Virus Diseases (from 1974).

[56] See: MRC Annual Reports, 1972-73, pp. 68-74 ('Research on liver disease: a review'), esp. 'Australia antigen and liver immunology', pp. 72-3; and 1975-76, 'Viral hepatitis', pp. 76-8, which ends with mention of Zuckerman, Almeida and Dane, without stipulating their sources of funding.

Zuckerman headed the WHO Viral Hepatitis Reference Centre, set up in 1974 at LSHTM.[57] As discussed in the previous section, he was able to build up an enormously varied sample bank, acting as a centre for information and a research source. He continued to survey the literature minutely and published a volume of abstracts in 1980.[58]

While successive MRC reports record few grants for research on hepatitis B, awards were made in 1979-80 to Zuckerman, to Sheila Sherlock at the Royal Free, Mortimer and Vandervelde at the PHLS Viral Reference Centre at Colindale, and Craske at the PHLS laboratory in Manchester, for research on non-A non-B hepatitis.[59] This was in response to a request from the DHSS, in the light of alarm over outbreaks associated with Factor VIII and also in a dialysis unit in London. At that time, Craske sat on a PHLS sub-committee on hepatitis, Zuckerman, Sherlock and Vandervelde on the latest DHSS advisory group on screening blood for hepatitis B.[60] This pattern suggests a feedback from expert committees to research, which (like the route from research to expert committees) was channelled through a few select individuals. Then in 1981-82, a report on the work of the MRC Committee on the Development of Vaccines and Immunisation Procedures included brief mention of

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[57] The reference centre was attached to the expert rather than the institution and moved with Zuckerman to the Royal Free Hospital Medical School when he became Dean there in 1989.

[58] Zuckerman, Decade of viral hepatitis: a resource I found invaluable in composing the first section of this chapter.

[59] MRC, Annual Report, 1979-80, p. 35.

[60] I am unsure of the date when the PHLS sub-committee was established.

possible vaccines against hepatitis B.[61]

By this time, a confidential Advisory Group on Hepatitis (AGH) had been set up by the DHSS.[62] This expert advisory group, established in 1980, was derived from two others: that on blood (the Maycock committee and its successors), and another which advised on hepatitis in dentistry in 1979.[63] The function of the post-1980 AGH will be discussed in Chapter 7. It is introduced here to demonstrate a striking continuity of institutional and personal affiliations, which can be found by tracing its links with previous advisory groups. This is a rather convoluted process, because it has not been possible to ascertain the group's membership in 1980, and therefore lists of members in 1992/3 have been used to give some indication of its earlier composition.[64]

One member of both the source groups who remained on the AGH

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[61] MRC, Annual Report, 1981-82, p. 57.

[62] Precise lineage and title of group varies according to source: one informant said it was the hepatitis sub-committee of the DoH Joint Committee on Vaccination and Immunization: J. Kurtz, interview, 20 Feb 1992; but the medical civil servant who dealt with hepatitis B gave blood/dentists committee derivation described in text and referred to it as Hepatitis Advisory Group: J. Hilton, interview, 30 Sept 1992.

[63] The latter will be discussed in the next chapter.

[64] Kurtz, interview, provided a list on the basis of a phone call he made during the interview to an unnamed colleague; I am grateful for this information. There were a dozen named members and two others the informant could not recall. Kurtz himself, a virologist at the Public Health Laboratory at the John Radcliffe Hospital, Oxford, was a member of the PHLS sub-committee on hepatitis. A nine-name list of AGH members is given in: UK Health Departments, Protecting health care workers and patients from hepatitis B, Recommendations of the Advisory Group on Hepatitis, August 1993 [17pp booklet, no publisher, printed for HMSO], p. 13.

in 1992/3 was Zuckerman. Dr R. Lane, now Director of the BPL, and Craske of Manchester PHLS, who both sat on the 1979-81 blood screening committee, were also members of the AGH in 1992/3. The central Public Health Laboratory was represented on the dentistry group by its Director, Professor Sir Robert Williams, and by Sheila Polakoff; and on the blood committee by Yvonne Cossart and later by Elise Vandervelde; while the 1992/3 AGH featured J. Heptonstall of the CDSC.[65] Maycock, Director of the blood transfusion service and BPL, provided input in both the earlier groups, but in the 1992/3 AGH the transfusion service was represented by M. Contreras, Director of NLBTC. Certain renowned 'experts' - professors in London teaching hospitals - appear on the 1992/3 AGH: besides Zuckerman of LSHTM, Banatvala of St Thomas's in the chair, Roger Williams of King's Liver Unit, and Thomas of St Mary's.[66] Dane, who sat on all three advisory groups on testing blood, was also a member of the AGH in the early 1980s.[67]

Conclusions

This chapter opened with a survey of the wide field of research on hepatitis B during the 1970s, when the new tool of

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[65] Plus two others in the Kurtz 1992 list: S. Young and N. Gill; but these do not appear in the 1993 source (see previous note).

[66] See n. 41 above for details.

[67] Dane's potted CV supplied with letter to author, 10 Nov 1993, gives '1970-1985: Member DHSS Hepatitis Advisory Group', expressing view of successive groups on testing for antigen (1972, 1975, 1981) feeding into hepatitis advisory group.

the antigen test opened up possibilities for clinicians to contribute small pieces of research, often epidemiological, while more scientifically oriented work was conducted by clinical researchers and scientists in a variety of settings. Much research was basic, but areas like test development which had a commercial application saw collaboration between service, academic and industrial sectors. Epidemiological research revealed patterns which might have informed policy, but drug use and sex as means of transmission were relatively neglected, while the construction of hepatitis B as a hazard in certain health care settings contined to dominate policy agendas. This is not surprising, as the Department of Health had responsibility in those areas. However that still leaves open to question the manner in which experts were chosen by the Department to interpret research findings and give advice on policy.

The section on London networks of researchers further explored the notions of varying sites and techniques of research, focussing on the antigen test and electron microscopy, showing how these featured in the research careers of a small number of researchers. One striking theme that emerged from this material was the role of reference centres as sample banks, and the exchange of samples of blood and serum between those engaged in different aspects of research work. Exchanges between those with special technical expertise, and those with reference expertise, built up networks which could be seen as an informal type of co-ordination of research. It was suggested that researchers located at reference centres were

in a stronger position to incur obligations and tended to become recognized as 'top' experts.[68]

The third section looked at more formal structures involved in co-ordinating research and policy. MRC committees surveyed research rather than forming policy, but there was overlap between these and DHSS committees in terms of personnel. The case of immunoglobulin was used to demonstrate how a leading researcher could be marginalized and treated as a technical resource, rather than influencing policy. By contrast, 'MRC type' experts carried weight as opinion leaders. If we take the more public advisory groups discussed in Chapters 4 and 5 - the Rosenheim and Maycock committees - together with the MRC committees that dealt with hepatitis, the dentistry group, and the later DHSS (and PHLS) hepatitis groups, there is clear continuity. Some members were chosen primarily because of their institutional position, such as head of BPL, others because of their expertise as medical scientific researchers. This chapter has tried to elaborate the means by which some researchers become experts with a policy role. These are the people in a position to mediate between research and policy.

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[68] A further clue may be provided by a 'Hepatitis Peer Group' established by Zuckerman in the 1980s, which is said to consist of a 'Who's Who' of hepatitis experts in the UK: anonymous informant, interview, 12 July 1991. Membership is unknown but the very existence of the group demonstrates that a select band of experts had emerged from the wide field of research and service work on hepatitis B in the 1970s.

CHAPTER 7: HEALTH AND SAFETY [1975-1990]

As chapters 4 and 5 showed, the test for hepatitis B impacted most immediately on two areas where the disease appeared as an urgent priority: the new problem of hepatitis in renal units, and the older problem of hepatitis in the blood supply. But the test presented a much wider opportunity, and a threat, for a whole range of workers in the health care sector and beyond. Prevalence studies - mentioned in Chapter 6 as a large part of the research application of the test - looking at groups of workers, such as surgeons, or blood laboratory technicians, established a higher rate of exposure to hepatitis B than in the population at large, opening the possibility for such workers to demand compensation for work-related attacks. On the other hand, routine screening (not anonymous as for prevalence studies) would reveal individuals who - previously unknown to themselves and employers - were hepatitis B carriers, exposing them to the risk of discrimination and loss of livelihood. There was a potential clash between the public health interest, perhaps best served by universal screening for health workers (as in renal units or the blood transfusion service), and the right of the individual to choose whether or not to undergo screening. And, as the previous chapter pointed out, policy on these matters was heavily influenced by the views of a limited circle of hepatitis 'experts', mainly doctors, themselves members of an occupational risk group.

Tensions between individual rights and the public health interest have been analysed for hepatitis B in the US by

William Muraskin, particularly in the cases of integration of retarded children who were known carriers into normal schools in the late 1970s, and the adoption of Asian children by American families, when the authorities failed to pass on information of carrier status of adopted children.[1] In those cases and in the broader arena of hepatitis B among health care workers,[2] Muraskin concludes that individual rights prevailed over the public health interest (in the schools case, in courtroom battles), to the possible detriment of numbers of people exposed to hepatitis B in the late 1970s and early 1980s. More important, in Muraskin's view, the policy of keeping quiet over hepatitis B meant that the public were deprived of an opportunity to debate issues that were later, more urgently, raised by AIDS: whether or not to test, whether or not to segregate, and so on. He blames the lack of action over hepatitis B on health care workers, as a high risk group which was able to exercise leverage on reporters who might otherwise have alerted public concern.

Muraskin's interpretation, being post hoc, is open to the benefits and the pitfalls of hindsight. The special hindsight provided by our current knowledge of AIDS is difficult to avoid, and it may be valid to ask (as Muraskin does) how the public and policy response to AIDS would have differed from what we experienced, if the public and policy response to hepatitis B had been different. But that is not the aim of

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[1] Muraskin, 'Controversy over the integration of retarded hepatitis B carriers'; Muraskin, 'Problem of Asian hepatitis B carriers in America'.

[2] Muraskin, 'Silent epidemic'.

this thesis. In this chapter it will be shown that in the UK in the 1970s and 1980s, groups of health workers were the chief source of pressure to take action on hepatitis B, as well as the main target of policy making after Rosenheim and Maycock. Their policy concerns were different from those Muraskin has discussed, and they may well have wished to avoid compulsory screening, but they kept hepatitis B on rather than off the policy agenda. Their struggles were over recognition of the danger of hepatitis B to health workers, compensation for those infected, and preventive measures to avoid infection. Such measures, which might be tedious, time-consuming and costly, were a matter for sometimes tendentious negotiations between laboratory workers, their bosses, and the Department of Health.

Finally, by way of introduction on the issue of individual rights versus the public health interest, it is instructive to look at two articles by Blumberg, separated by a decade.[3] In the earlier of these two pieces, Blumberg marshalled the available evidence and concluded that compulsory screening, of health workers or others, would be inadvisable. Tests would show which individuals carried the surface antigen, but it was becoming clear that not all carriers were equally infectious, and there was still no means of identifying those who were particularly infectious. Carriers would be stigmatized, might lose their jobs and suffer insurance problems, but could not

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[3] B. S. Blumberg, 'Bioethical questions related to hepatitis B antigen', American Journal of Clinical Pathology, 65 (1976), 848-53; B. S. Blumberg, ' The Daedalus effect: changes in ethical questions relating to hepatitis B virus', Annals of Internal Medicine, 102 (1985), 390-94.

be helped medically. Perhaps they could be instructed how to avoid passing the virus on to family members, but even this area was riddled with uncertainties. The drawbacks for the individual far outweighed the benefit to others, at this stage. In the later paper, Blumberg sees greater benefits in testing, chiefly because further differentiation was now possible; those carriers of the surface antigen who also tested positive for the 'e' antigen were likely to be more infective. With the additional tool of the 'e' antigen test, and the advent of a vaccine for hepatitis B, the scales had swung in favour of wider testing - though not necessarily universal testing of health workers. There was still no treatment and still the risk of stigmatization; along with issues of testing for AIDS and other infectious diseases, the argument over hepatitis B testing remained unresolved.

Hepatitis as a laboratory hazard

In hospital laboratories, blood traditionally enjoyed a favourable image: compared with other bodily products which laboratory workers had to analyse, such as faeces or vomit, blood was regarded as relatively sterile. Even as the renal unit outbreaks were making their dramatic impact, a report from a clinical chemistry laboratory reflects the enduring power of this image:

> ... it is remembered that few diseases are transmitted by contact with blood and that the incidence of serious disease such as serum hepatitis, although a recognized hazard of laboratory work in hospitals, is undoubtedly

low.[4]

Conditions for handling blood were uneven, varying from one laboratory to another depending on the consultant pathologist or bacteriologist in charge, and on the local staff ethos. One informant gave a graphic account of poor attention to safety prior to the renal unit outbreaks:

> Standards of handling blood were awful in pathology throughout the country. I think that people must have thought that blood was not a source of infection. The types of containers that were used, the stoppers that were in them, I mean they leaked ... it was impossible to open them without getting stuff all over your hands. People didn't wear gloves, so it was very common for them to be getting blood and serum on their hands... It wasn't uncommon for somebody, some lazy bod, to send the blood specimen in the syringe with the needle still on the end.[5]

The renal unit hepatitis outbreaks changed matters drastically. The same informant described the increased interest in safety with regard to hepatitis B, following the renal unit outbreaks:

> People began to take an interest in safety and I think the first things that happened were we improved the blood collection tubes, and people got containers that didn't leak, and they got them with lids that didn't splatter the specimen all over your hands when you took it off. I mean, there were actually some where you had to get your nails inside to get them [off] ... it was just impossible not to get the blood on your fingers.[6]

In this passage describing the improvements, the informant returned to the previous poor conditions, which clearly haunted him. He also commented that it was still (in 1991) common practice for technicians to work without gloves in some

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[4] I. W. Percy-Robb, J. Proffitt and L. G. Whitby, 'Precautions adopted in a clinical chemistry laboratory as a result of an outbreak of serum hepatitis affecting hospital staff', Journal of Clinical Pathology, 23 (1970), 752.

[5] B. Gee, interview, 21 June 1991.

[6] Ibid.

laboratories.[7] There seemed to be a view that microbiology laboratories had tighter controls than biochemistry or haematology laboratories, while the morbid anatomy or pathology laboratories carried higher risks because of the nature of their work.

This impressionist view was supported by a series of surveys under the auspices of the Association of Clinical Pathologists throughout the 1970s, which indicated that the risk of hepatitis B in clinical laboratories was greatest for biochemistry and haematology technicians; it was suggested in 1975 that there was room for improvement in safety standards in these areas.[8] By the end of the decade, a fall in rates led Grist, the author of these surveys, to conclude that safety standards had improved and the risk of hepatitis was now small. Indeed Grist remarked with regard to the range of infections possibly transmitted by laboratory work:

> ... the case of malaria gives a salutary reminder that hepatitis is not the only infection which workers risk from parenteral exposure. Overpreoccupation with the risk of hepatitis may be dangerous if it diverted the attention away from a broader vigilance.[9]

Some laboratory workers were incensed by the underplaying, as they read it, of the hepatitis risk. The pathologists'

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[7] With some reason; apparently gloves can cause skin problems if worn all day. In some laboratories, gloves were not necesssarily worn, even when serum specimens were 'bright yellow': personal communication from former laboratory technician, 12 Oct 1991.

[8] N. R. Grist, 'Hepatitis in clinical laboratories: a three-year survey', Journal of Clinical Pathology, 28 (1975), 255-9.

[9] N. R. Grist, 'Hepatitis and other infections in clinical laboratory staff, 1979', Journal of Clinical Pathology, 34 (1981), 658.

surveillance had been undertaken by postal questionnaire asking for reports of cases of hepatitis (and subsequently other diseases also) in laboratory workers: workers were not screened for markers of hepatitis B infection, current or past. Among the long-term risks associated with hepatitis B (which usually went undetected), were cirrhosis and cancer of the liver. The conclusions of the Association of Clinical Pathologists' survey were to some extent undermined when a clinical pathologist died of liver cancer at just the time when colleagues were suggesting that hepatitis B was no longer a problem in clinical laboratories.[10] In the view of laboratory technicians, the disease remained a highly dangerous hazard, whether or not rates of work-related cases fell due to careful safety precautions.

The union which represented most blood laboratory technicians, the Association of Scientific, Technical and Managerial Staffs (ASTMS), successfully campaigned in the mid-1970s for hepatitis B to be scheduled as an industrial disease.[11] Cover was limited to those who worked in close and frequent contact with blood and blood products, or in close and frequent contact with patients who might be carriers of viral hepatitis.[12] This 'close and frequent' proviso, inserted

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[10] Gee, interview; the link with hepatitis B in this case could not be proved but had apparently entered the folklore.

[11] J. Williams, 'Viral hepatitis: prescription first result of continuing campaign', Medical World, February/March 1976, pp. 12-13; Williams was a member of ASTMS National Executive Committee.

[12] DHSS, Viral Hepatitis, Report by Industrial Injuries Advisory Council in accordance with Section 141 of the Social Security Act 1975 on the question whether viral hepatitis

because it was often impossible to identify accurately the source of a particular infection (bearing in mind the long incubation period of hepatitis B), excluded many health workers and also groups outside the health service, like the police or other service workers, who were concerned about contracting the disease in the course of their duties.[13] However, it could in theory apply to many doctors, dentists and nurses, as well as laboratory workers who handled blood.

During the second half of the 1970s, the struggle over safety in laboratories centred on microbiological hazards. As a result of a combination of the 1974 Health and Safety at Work Act, and the Working Party on Laboratory Use of Dangerous Pathogens, the DHSS established an expert working party under the chairmanship of Sir James Howie (head of the PHLS) to produce a code of practice for the prevention of infection in clinical laboratories.[14] Health unions would have preferred that such a group fall under the Health and Safety Executive, since there had been a long history of the DHSS failing to act

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should be prescribed under the Act (London: HMSO, 1975), p.12.

[13] Telephone engineers servicing telephones for patients on home dialysis were mentioned by Rosenheim as an instance of 'people whose duties take them into the houses of such patients' and who were worried about contracting hepatitis. Rosenheim commented that risks were very small, advice and information was available from the director of the dialysis unit concerned, and for added reassurance patients could install 'plug-in' phones which could be removed for servicing: Rosenheim Report, p.40.

[14] DHSS, Code of Practice for the Prevention of Infection in Clinical Laboratories and Post-mortem Rooms, Department of Health and Social Security, Scottish Home and Health Department, Department of Health and Social Services Northern Ireland, and Welsh Office (London: HMSO, 1978) ['Howie Code']; p.iii gives lineage of this working party.

on its own reports. When the Howie Code (as it came to be known) was finalized, laboratory workers first welcomed it, and then became incensed with the delay in publication, which they attributed to the usual DHSS reluctance to commit itself to anything that might incur expenditure, coupled this time with opposition from some professional interests. So the draft report was published in Medical World, the journal of the Medical Practitioners' Union which had joined ASTMS.[15] This move, together with an incident when smallpox escaped from a laboratory, apparently prompted the official publication of the Howie Code.[16]

According to the union, DHSS concern over costs coincided with the outrage of laboratory bosses 'when HSE [Health and Safety Executive] inspectors started to give them a few basic lessons in safe systems of work', leading to a further attack on the Howie Code.[17] An attempt to reduce the hazard status of hepatitis B (from category B1 or B2, high risk, to C, low risk), was interpreted by ASTMS as a means of undermining the

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[15] 'The prevention of infection in clinical laboratories', Medical World, 115, 2 (Dec 1977), 5-12; 'The prevention of infection in clinical laboratories (2)', Medical World, 116, 1 (Jan 1978), 7-11; 'The prevention of infection in clinical laboratories (3), Appendices', Medical World, 116, 2 (Feb 1978), 7-10. See also: 'The Howie Report', Medical World, 116, 2 (Feb 1978), 6, for comment on publicity for the report.

[16] Dane and Gee, interviews; the latter mentioned a case of smallpox at St Mary's as precipitating the publication of the Howie Code, while others have mentioned an escape of smallpox from a laboratory at LSHTM.

[17] ASTMS Health and Safety Office Special Report, The risk of hepatitis to laboratory workers: the case against the attempt to downgrade safety standards in laboratories testing hepatitis B virus specimens (London: Association of Scientific, Technical and Managerial Staffs, 1980), p. 7.

Howie Code. The union fought back with a detailed case against downgrading hepatitis B,[18] as a counter to the case for downgrading put forward by a Joint Working Party headed by Zuckerman.[19] As an example of the linkage between hazard classification and expenditure, the union reported from their members' response to consultation on the debate: 'The rumour of reclassification has already led to the cancellation in one Area Health Authority of a number of safety cabinets for B2 work'.[20] There was anger over the expert committee's use of falling numbers of hepatitis cases among laboratory staff to justify downgrading the hazard: 'Nobody seems to be arguing that because smallpox is no longer the cause of disease among laboratory staff (except in unsafe laboratories) we can argue that it should be reclassified' - a telling jibe, in view of a number of cases of escape of smallpox from laboratories, with sometimes fatal consequences.[21]

One of the union's proposals urged that: 'Any action that needs to be taken should henceforth be the responsibility of

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[18] Ibid; this is a 37 page document, with four appendices.

[19] Ibid, Appendix 1, Stated case for downgrading hepatitis B virus specimens (B2) to category C, paper prepared by the Joint Working Party of the Association of Clinical Biochemists, Association of Clinical Pathologists, Institute of Medical Laboratory Scientists, and Royal College of Pathologists, 29 April 1980, 10pp. including references and tables. Members of the Joint Working Party were Zuckerman, Waterson, Banatvala, Vandervelde (mentioned in previous chapters), and Dr S. Clarke, Consultant Virologist, Public Health Laboratory, Bristol. According to ASTMS, many of their members who belonged to the Institute of Laboratory Medical Scientists disagreed with the Joint Working Party's views.

[20] ASTMS, Risk of hepatitis to laboratory workers, p. 34.

[21] Ibid, idem.

the Health and Safety Commission not the DHSS'.[22] The union felt it was contrary to the best interests of promoting health and safety, that the DHSS should retain control over matters like the safety categorization of a biological hazard. Such decisions should be removed from the DHSS, with its overriding concern over cost-cutting in the NHS, to the Health and Safety Commission, argued the union. Under the Health and Safety at Work Act of 1974, the Howie Code was implemented with proper inspection, but the Control of Substances Hazardous to Health Act (billed in 1988, enacted in 1990) and the removal of Crown Immunity again stirred Departmental unease. The end of the 1980s witnessed the DoH delaying publication of a revised version of the Howie Code, probably for similar reasons of anxiety over cost as in 1978. Although there were two DoH observers at the Health Services Advisory Group which revised the Howie Code, they insisted on consultation throughout the Department prior to publication, a lengthy rigmarole which delayed progress for two years from 1989 to 1991.[23] Union views that the DoH, as employer, should not have the final word on health and safety appeared to be vindicated.

Health workers in contact with patients

Although there was never universal screening of health staff, various studies, in the UK and elsewhere, had shown that

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[22] Ibid, p.36.

[23] Gee, interview; the Health Services Advisory Group was a tripartite body composed of employers (health authorities), employees (trade unions, RCN and BMA), and the Health and Safety Executive.

surgeons and dentists ran a risk of contracting hepatitis B from patients and transmitting it to patients.[24] However, the issue of hepatitis B and health service staff, including nurses, remained shadowy throughout the 1970s. Infection control guidelines, produced in response to renal unit outbreaks, could be applied to any situation where a risk of hepatitis transmission seemed likely - but the problem lay in identifying that risk. Even in mental health institutions (MHIs), perhaps the most notorious loci of institutional infection, there seems to have been little policy initiative to stamp out infection from patients to staff or vice versa.[25] Within the hospital setting, renal units came to be seen as a special case; elsewhere in the hospital, in wards and operating theatres, life returned to normal although the aftermath of the renal unit outbreaks continued to resonate for a while.

In a few instances, there is evidence of the tendency to 'blame others' especially characteristic of responses to sexually transmitted diseases (syphilis, AIDS) or of major epidemics (plague, cholera). It seems perhaps anomalous that

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[24] Zuckerman, Decade, gives 59 abstracts under the heading 'occupational hazard', of which about 15 appear to originate from the UK; many of these are by Grist on the clinical laboratory risk. At this date there were few studies linking surgery and hepatitis B; on dentistry, see: H. D. Glenwright, H. D. Edmondson et al, 'Serum hepatitis in dental surgeons', British Dental Journal, 136 (1974), 409-13; G. F. Goubran, H. Cullens et al, 'Hepatitis B virus infection in dental surgical practice', British Medical Journal, 1976 (2), 559-60.

[25] Notorious because of the Krugman experiments (see Chapter 2); through the 1970s, there was uncertainty over possible modes of transmission in the MHI setting, with debates over presence of virus in saliva, given that biting was commonplace.

this pattern should appear in relation to hepatitis B in the health service setting, with only a limited number of cases, and transmission known to be mainly via blood. Yet in Colin Douglas' book, the agent of transmission in the fictional Edinburgh hospital was a nurse who had slept with several junior doctors: the promiscuous female as angel of death.[26] Probably many dentists and surgeons were more alarmed over the risk of transmission from patient to practitioner than the contrary risk. Since patients were not screened, certain categories such as 'drug addicts' were seen as a potential hepatitis hazard and avoided by some practitioners. The few accounts given by patients who were known hepatitis B carriers suggest that avoidance was an unwritten policy among dentists in the 1970s.[27]

At the higher levels of the dental profession, there was concern that certain patients might become 'dental lepers', more often due to unconfirmed suspicion that they might be hepatitis carriers rather than known carrier status. A report by an expert group to the Chief Medical Officer and Chief Dental Officer in 1979 sought to ensure that all patients would receive appropriate treatment.[28] Paradoxically, known carriers could continue to be treated in normal practices, with the use of precautions such as gloves, masks and careful

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[26] Douglas, Houseman's tale; see discussion in Chapter 4.

[27] Mr X, interview, 9 Feb 1993 (see 'A surgeon's tale' below); Zuckerman files, London School of Hygiene and Tropical Medicine, account by female patient.

[28] DHSS, Hepatitis in Dentistry. Membership was drawn from university dental departments, reference laboratories, blood services and the central PHLS.

disinfection to avoid contamination with the patient's blood and saliva. These known carriers would include blood donors who had been informed that their blood carried the hepatitis surface antigen. On the other hand, the report recommended that certain categories of patients should be treated in hospital dental departments. In addition to those with apparently infective jaundice, those with renal failure on dialysis, and those receiving immuno-suppressive therapy (for instance, transplant patients), the list included categories that had appeared in the literature repeatedly. These were haemophiliacs, patients in institutions for the mentally handicapped, and known drug addicts.[29] Clearly, the concept of 'risk groups' was operating, de facto though not in name.

There is a curious aspect to this division - a division which seems to reflect the prejudices of dentists that led to the setting up of the working party in the first place. Dentists could be referring certain patients to hospital departments on the basis of their supposed membership of a 'risk group', while continuing to treat known carriers of hepatitis B (with caution) in their surgeries. In normal practice, it was recommended that dentists leave hepatitis carriers to the end of a day's list, and disinfect equipment thoroughly afterwards.[30] Where carriers were treated in hospital dental

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[29] Ibid, p. 2; 'known drug addicts' referred to those registered with a doctor or clinic for prescriptions of heroin. It seems to have been assumed that members of the medical and dental professions could share knowledge of a patient's imputed hepatitis B status; confidentiality was scarcely discussed.

[30] Ibid, idem.

departments, extremely careful precautions might be employed, as in Cardiff's 'dental isolation unit'.[31] Here, disposable instruments were used as far as possible, high speed aerosol producing drills avoided, and no ordinary assistants allowed in the isolation unit. Two dental surgeons took turns at acting as operator and assistant, wearing paper gowns, masks and hats, protective spectacles and two pairs of rubber gloves - and no doubt terrifying the patients. Even a modified version of this regime would be expensive and troublesome for the average dentist, yet they were urged to treat all patients as potential hepatitis risks.

When we turn from the risk presented by patients, to the risk of dentists and surgeons transmitting hepatitis B to patients, the story throughout the 1970s is chiefly one of denial: this was supposed to be a rare or non-existent occurrence. In the 1970s, Dane and Polakoff gradually established that surgeon-to-patient transmission must have been the cause of certain cases of hepatitis B in patients (often attributed to infected blood transfusions). As described in Chapter 6, two DHSS advisory groups, that on testing of blood and that on hepatitis in dentistry were reformed into a new, unitary Advisory Group on Hepatitis in 1980; this was a concentration of expertise on blood, virology and epidemiology.[32] One of the first tasks of this expert advisory group was to make recommendations on how to deal with the potential problem of

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[31] D. Adams and R. Zwink, 'Treating Australia antigen positive patients: practical experience', British Dental Journal, 141 (1976), 341-3.

[32] J. Hilton (Department of Health), interview, 30 Sept 1992.

carriers within the health service. The resultant guidelines on hepatitis B and NHS staff issued by the Chief Medical Officer of Health on the last day of 1981 were reassuring.[33] Health authorities were advised that staff in departments other than renal units should not be barred from work if they were found to be hepatitis B carriers; they should be given advice on how to avoid transmitting the infection, but otherwise their work need not be limited. Only if they had actually transmitted the disease should their work be curtailed:

> In the very rare instances where a member of staff who is a carrier appears to have been the source of hepatitis B infection in patients, that individual should perform only those activities in which the possibility of further transfer is remote; surgeons should not carry out operations but may continue non-operative work with patients, including taking blood or giving injections, using suitable precautions.[34]

Since health staff were not routinely screened, the number of carriers among them was subject to speculation; here, it was suggested that several hundred would be involved. Presumably the AGH foresaw great problems if they counselled a policy of screening staff and removing such a significant number of carriers from 'hands-on' work in the NHS. They recommended against screening either patients or staff.

The AGH felt these cases were rare, and only occurred when the surgeon in question was a highly infective carrier, involved

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[33] DHSS circular letter CMO (81) 11, from H. Yellowlees, Chief Medical Officer to Regional Medical Officers and Area Health Medical Officers &c, 31 December 1981, 'Hepatitis B and NHS Staff', with attached 2-page memo, 'Guidance on hepatitis B surface antigen carriers among NHS staff'.

[34] DHSS, 'Guidance on hepatitis B ... carriers among NHS staff', p. 1.

in surgery deep in the abdomen or chest where needle pricks and scalpel nicks were more common - gynaecological or cardiac surgery. Had they demanded that such surgeons be screened, the surgeons in turn might have demanded the screening of all patients, which would be costly and perhaps politically embarrassing. Dane records:

> In my experience most surgeons did not hold back from operating on HBsAg positive [i.e. hepatitis carrier] patients or patients in 'high risk' categories. I could see that this attitude might not remain if regular screening of surgeons was introduced and they were threatened with loss of their professional life as a result of a blood test. I sensed the attitude of surgeons to be: "We will put up with the substantial risk of contracting hepatitis B from our patients if they will put up with the very small risk of being infected by a carrier surgeon before he is identified as a transmitter".[35]

In the light of subsequent cases of transmission from surgeons to patients, Dane was slightly defensive in his recollections about the position taken by the group, but he felt that it was a reasonable position to take at that time, knowing what they knew then.

Developments in the 1980s following the introduction of the hepatitis B vaccine will mainly be discussed in the next chapter, but it seems appropriate to mention here a review of hepatitis B linked with surgery, covering the period 1975 to 1990, i.e. before and after the vaccine became available.[36] According to this 1991 survey, the vaccine made little impact

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[35] D. S. Dane, letter to author, 22 Oct 1992, p. 5.

[36] J. Heptonstall, 'Outbreaks of hepatitis B virus infection associated with infected surgical staff', Communicable Disease Report, 1,8 (19 July 1991), R81-R85. This includes reference, among others, to: S. Polakoff, 'Acute hepatitis B in patients in Britain related to previous operations and dental treament', British Medical Journal, 293 (1986), 33-6.

on the frequency of outbreaks of surgery-associated hepatitis B, which averaged about one per year throughout the period under review: two outbreaks detected in 1990 had prompted the review. Most outbreaks had been reported in medical journals, others had not received published notice, but in any case the data received by the Communicable Disease Surveillance Centre allowed further details to be elucidated. Twelve outbreaks were detailed (11 involving surgeons and one involving a perfusion technician), affecting 91 patients and four contacts - but as the report pointed out, cases without jaundice were only traced in three of the more recent outbreaks, via serological surveys; thus the true total of cases was possibly nearer to 200. Almost certainly there were other, unreported, instances of surgical transmission of hepatitis B during this period. The majority of the outbreaks surveyed arose either in gynaecology,[37] or cardiothoracic surgery, but general surgery was implicated in some cases.

Three out of nine surgeons identified as carriers with the 'e' antigen had received all or part of a course of vaccine, presumably after they had already, unknowingly, become carriers. Testing for hepatitis-related antigen was not usually conducted before vaccination; conversion to antibody seropositivity was not always checked afterwards.[38] Testing

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[37] Apparently including obstetrics, as there is mention of forceps deliveries in two cases.

[38] Testing prior to vaccination could have saved about 9 months in the process of discovering those rare instances where a surgeon was positive for the surface and maybe also 'e' hepatitis B antigens; but it was not carried out, probably because (a) it might seem to contravene the 1981 guidelines and (b) it might inhibit staff from coming forward for

unrelated to vaccination still followed the pattern laid down in the 1981 guidelines: workers were not tested until patients had developed jaundice following treatment. Strenuous efforts appear to have been made to trace other patients operated on by the surgeon implicated in the initial cases, but testing of the surgeon could still be delayed:

> In most of the outbreaks reported here, specimens were not requested from surgical team members until two or more patients had developed acute icteric HBV [hepatitis B virus] infections within six months of surgery and the association between them had been recognised. Many patients with a history of surgical exposure have also received blood transfusions, and it has been usual to exclude transfusion acquired HBV infection before investigating the possibility of HBV transmission from an infected health care worker.[39]

To allow more rapid detection and reduction of hepatitis B transmission, the 1991 survey proposed that whenever a patient developed hepatitis B within six months of surgery, all members of the surgical team involved should be asked to undergo testing. Such investigations should be initiated where only one patient showed signs of infection; previously, at least two cases had to be observed before action was taken. But Dr Julia Heptonstall, author of this survey, while encouraging universal vaccination for all surgeons, stopped short of recommending testing for this group. The problem would then remain: what to do about those individuals who failed to respond to the vaccine because they were already carriers?

As matters stood during the 1980s and into the 1990s, the co-

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vaccination: D. S. Dane, letter to author, 30 Nov 1992.

[39] Heptonstall, 'Outbreaks', R83-4.

operation of health workers who might be a source of infection was crucial in containing hepatitis B in the health sector. This is clearly revealed in an internal inquiry conducted by a hospital which discovered in 1990 that two of their patients had developed hepatitis B following cardiothoracic surgery.[40] A newly appointed surgeon (a registrar) claimed that he had received hepatitis B vaccine, but tests by the Occupational Health Department revealed that he had not developed immunity and was in fact a carrier of the 'e' antigen. By the time his test results came through the surgeon had already taken part in one operation which resulted in the patient acquiring hepatitis B (later cleared) - but nobody knew of this infection until later, due to the long incubation period of the disease. The surgeon withdrew consent to further tests, as he was entitled to do under the 1981 guidelines, which were still in place; the Director of Occupational Health relayed this decision to the Consultant in Virology, who interpreted it as requiring confidentiality. The surgeon's carrier status was therefore not revealed to anyone else for a period of five months.

Against the advice of an outside consultant whom he saw, the surgeon continued to operate, believing that careful adherence to safe procedures (including double gloving) would prevent transmission of the virus. He was unaware that he had already infected one patient: subsequently he infected a second. The

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[40] 'Report of the internal inquiry into the hepatitis B incident', typescript, 1990. As this internal inquiry was made available to me confidentially, I am following normal practice in not revealing the location of the hospital.

fact that these two cases had occurred only came to light at a meeting called on another issue; the hospital's Control of Infection Committee had had no knowledge of the second case. The Director of Occupational Health revealed the surgeon's carrier status, which had been kept confidential, and the surgeon was suspended pending investigation. The hospital's internal inquiry panel found that DoH guidelines had been adhered to, but had clearly proved inadequate: therefore they recommended review of these guidelines by the DoH as soon as possible.

The case just cited illustrates the effect of the 1981 guidelines on hepatitis B and NHS staff, nearly a decade later - what clearly appeared to the inquiry panel as a mistaken weighting of the balance in favour of the rights of the individual surgeon to keep his carrier status confidential, against the public health interest.[41] It should be stressed that in all these cases, where two or more patients had developed jaundice, efforts were made to trace infection, either to a transfusion source or (if that failed) to the operating surgeon. A surgeon's rights to avoid testing and to deny knowledge of his carrier status to colleagues most closely concerned, such as the control of infection officer, could no longer be protected when such an outbreak had occurred. Although patients who had been infected received no redress other than an apology, future protection of other patients became paramount once a surgeon had proved infectious.

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[41] The same balance was observed in relation to testing health workers for HIV: Berridge, History of the present, shows professional self-regulation was relied on for AIDS.

A surgeon's tale

Tracing of a carrier surgeon did not mean loss of all rights to confidentiality: when cases were published, names and locations were not mentioned.[42] One carrier surgeon agreed to be interviewed for this study, on condition I adhered to the same strict code of confidentiality. Mr X learned in August 1978 that he was hepatitis B positive. Seven patients who had either developed jaundice or were diagnosed as hepatitis B positive had been operated on by Mr X in a six-month period, presumed to be the period when he was himself incubating the disease; no patients had been infected during the six months before and six months after the incubation period, despite his involvement in similar numbers and types of operation. Mr X had probably acquired hepatitis B during an operation on an infected patient, and then passed it on to others.[43] But he was told by a senior officer at the Department of Health that 'the only victims in this are the patients'.[44] At area, regional and departmental levels, he felt, officials were all 'watching their backs', fearing that patients would sue. The local Medical Officer of Health wrote to the General Medical Council asking for Mr X to be struck off the Medical Register; though this was not taken up, it registered as a bitter blow.

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[42] Again, this parallels the new recall procedures for AIDS, as Berridge has pointed out.

[43] In the opinion of experts such as Zuckerman, Polakoff and Almeida: Mr X, interview. He quoted Roger Williams' (King's Liver Unit) calculation that the risk of a doctor acquiring hepatitis B from a patient was 22 times greater than that of transmission from doctor to patient.

[44] Mr X, interview.

Unlike other surgeons caught in the hepatitis B trap, Mr X refused to give up operative work entirely and demanded the right to follow a normal career path. Once identified, hepatitis carrier surgeons were encouraged by employers and the DoH to switch careers, away from patient contact, to research or administration. Against great opposition, Mr X carried on as a surgeon, developing a sub-specialty which used non-invasive techniques. Only after a protracted legal struggle, with backing from the British Medical Association (BMA), did Mr X gain some job security, in the shape of a personal senior registrar post. From 1985 to 1991 he battled to persuade his employing authority to establish a personal consultant post for him. This was finally secured with intervention at the highest level, involving a friend in the House of Lords, and ministerial dispensation.[45] Mr X had survived as a clinical practitioner in his chosen specialty, creating a precedent not only for other hepatitis B carriers in the NHS but for AIDS sufferers too. It had been a long and exhausting journey. Mr X compared dealing with the Department of Health with 'walking through treacle'; he said he found officials defensive, not entrepreneurial or imaginative, more afraid of the press than of wasting a doctor's career.

Elements in the personal side of the surgeon's story, such as problems over mortgages and life insurance, are fairly representative of the experiences of other victims of

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[45] The Secretary of State dispensed with the requirement to advertise the post (a power which was rarely used), in case someone else was appointed, using up the money set aside to pay Mr X.

hepatitis B. Other aspects were affected by his professional status. For example, when hepatitis B vaccine became available, a course from the first batch of thirty doses in the UK was given to Mrs X, who was not a hepatitis carrier; and the two children born subsequently were both immunized at birth. Mr X was offered interferon when its use for hepatitis B was still very experimental, but declined, preferring not to become 'a laboratory animal'. Ten years after his initial infection he experienced a bout of illness, which simulated some of the effects of interferon treatment, and he was then found to have converted from 'e' antigen to 'e' antibody positivity, with lowered surface antigen levels. Now a mild rather than an infective carrier, he could 'do anything other than give blood'.[46]

The extreme bitterness which this surgeon evinced over the way that he had been treated presumably reflects the high career expectations which the long training and professional ethos of hospital medicine inculcates. Although Mr X received backing from the BMA, it came belatedly; meanwhile, fellow doctors in his immediate vicinity, such as the local Medical Officer of Health, as well as his employers, wanted to get rid of him. The fraternity of hepatitis experts suported him, but even with their help, his battle with the authorities lasted thirteen years. This case lends support to the view that carriers tend to be victimized, perhaps more so in the case of health workers since they are liable to lose their job. On

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[46] Dane had predicted this conversion when Mr X was first diagnosed as a carrier, and had told him it would happen in about ten years time: Mr X, interview.

the other hand, great sympathy and understanding was shown towards the carrier by the experts who perhaps identified with his plight. Whether this case influenced decisions over the handling of health workers with AIDS is uncertain.

Precautions and emergency action

Much of this chapter has been concerned with debates over screening, but there has been mention of other preventive measures. In laboratories, on wards and in operating theatres and special dental units, wherever there was an enhanced risk of hepatitis B transmission, precautions were supposed to be taken by health staff. Those who handled blood samples suspected of containing the virus, or those who cared for patients thought to be incubating or carrying the disease, could protect themselves to some extent by the use of physical barriers, and could protect others by meticulous cleaning and disinfecting of contaminated implements and surfaces.[47] How far such measures offered real protection is open to question. White coats, or elastoplast over cuts, scarcely constituted serious barriers to a microorganism as persistent as the hepatitis B virus, but they served as a reminder of the worker's vulnerability and perhaps reinforced the need to observe a series of other, much stricter, precautions.

Laboratory workers, as we have seen, were often in the vanguard of these tighter hygiene measures. For example, a

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[47] See: COHSE (Confederation of Health Service Employees) Factsheet, 'Hepatitis B: Ensuring health staffs are protected' (No date, c.1988)

group from the clinical chemistry laboratory at the Edinburgh hospital affected by the renal unit outbreak of hepatitis B drew up their own list of hygiene measures in 1970, adapting and amplifying those proposed in the 1968 PHLS guidelines.[48] The Edinburgh procedures included careful labelling and packaging of samples, use of pipettes with rubber suction bulbs rather than mouth pipettes, techniques to avoid creation of aerosols during cetrifugation, and careful disinfection of the automatic analyser. Gloves were worn all day except for meal and tea breaks which were taken outside the laboratory. Procedures for reporting accidents were improved: these, and the observation of safety measures, were underwritten by the appointment of a safety officer from among the ranks of laboratory technicians.

We can trace a reciprocal interaction between laboratories and the centre, from the 1968 PHLS guidelines, through the 1972 Maycock and Rosenheim recommendations, to the Howie Code of 1978 and beyond. Bodies of experts drawing up codes of practice relied heavily on the 'best practice' examples currently on offer around the country, whether or not they were published as in the Edinburgh case. Implementation varied widely, probably depending at first on distance from foci of infection such as renal units. Standards gradually shifted through the 1970s and 1980s, though not without a rearguard action from some laboratory bosses and the DHSS/DoH.[49]

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[48] Percy-Robb et al, 'Precautions adopted'

[49] See discussion on wrangles over the Howie code, above.

Tighter precautions made demands on doctors requesting tests; on individual laboratory workers and safety representatives; on clinical laboratories which had to provide extra resources; and on waste disposal services. The greatest individual responsibility for safe handling of samples, possibly infected with hepatitis B, was undoubtedly placed onto laboratory workers. The reduction over this period in the number of cases of hepatitis B among such workers may indicate successful adoption of stricter hygiene precautions - measures which to a large extent the workers fought for and defended - supported by the safety representatives' role.

At a local level, enquiries about hepatitis B received by virologists working in public health laboratories ranged from anxious requests from GPs concerning the differentiation of hepatitis A from B, through to hospital control of infection officers asking where to obtain immunoglobulin for a health worker involved in a needlestick injury, a common accident in the health service setting.[50] Specific immunoglobulin, developed in the early 1970s, continued to be recommended as an emergency treatment for accidental exposure to hepatitis B right through into the period when vaccine became available.[51] Its efficacy was very much a matter of debate at first, as we have seen,[52] but as the only possible salvation in case of

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[50] From papers of J. B. Kurtz, Public Health Laboratory, John Radcliffe Hospital, Oxford; I am grateful to Dr Kurtz for loaning me these papers. No specific cases will be cited.

[51] Kurtz papers, including minutes of several PHLS hepatitis sub-committee meetings.

[52] As discussed in Chapter 6.

accidents, it gradually won backing from the DHSS. It also came to be recognised as an effective means of reducing the chance of a baby born to a hepatitis B carrier mother acquiring the disease at birth, and with it the high risk of liver cirrhosis or cancer in early adult life.[53] For those unfortunate enough to have become carriers, the only medical solution on offer was interferon, used experimentally for hepatitis B from 1982 onwards, with uneven results.[54] From 1982, a vaccine was available, but this failed to transform the health and safety picture for at least the first decade, as the final chapter will show.

Interim guidelines brought out by the DoH in 1990 linked precautions against hepatitis B with those against HIV in a clinical setting.[55] However, the DoH finally updated the 1981 guidelines on hepatitis B and NHS staff only in 1993, in a substantial booklet drawn up by the Advisory Group on Hepatitis.[56] Reference to 'a number of well-documented outbreaks of hepatitis B following transmission from health

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[53] S. M. Wheeley, E. Boxall and M. J. Tarlow, 'Prognosis of children who are carriers of hepatitis B', British Medical Journal, 294 (1987), 211-13.

[54] Group B, interview; for the earlier history of interferon, see: T. Pieters, 'Interferon and its first clinical trial: looking behind the scenes', talk given to Wellcome Trust Twentieth Century Medical History Group at the Royal College of Physicians, London, 11 Feb 1992.

[55] Department of Health, 'Guidance for clinical health care workers: protection against infection with HIV and hepatitis viruses' (London: HMSO, 1990)

[56] UK Health Departments, Protecting health care workers and patients from hepatitis B, Recommendations of the Advisory Group on Hepatitis, August 1993 [17pp booklet, no publisher, printed for HMSO]

care workers to their patients'[57] perhaps indicates that production of the booklet was partly prompted by Heptonstall's 1991 report, which drew together published and unpublished cases that had come to the notice of the CDSC.[58] Heptonstall was a member of the Advisory Group on Hepatitis in 1993.

Leaving aside recommendations on immunization, which will be discussed in the next chapter, a main emphasis of the 1993 guidelines is the high risk of an 'e' antigen carrier infecting patients, and conversely the low risk of a carrier who does not have this antigen infecting patients.[59] Despite the low risk in all but the tiny minority of cases, 'routine infection control measures' must always be followed by all health care workers.[60] Special restrictions on 'exposure prone' work are ruled for those who carry the 'e' antigen, but surface antigen carriers are relieved of such restrictions, including those previously in force for work in renal units.[61]

In the careful advice on handling of cases of health workers found to be hepatitis B carriers, with great emphasis on

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[57] Ibid', p.3, para. 1.3.

[58] Heptonstall, 'Outbreaks', discussed earlier in this chapter.

[59] Cf: Blumberg, 'Daedalus effect'; the 'e' antigen, discovered in 1972, was gradually linked with high infectivity.

[60] UK Health Departments, 'Protecting health care workers', p. 4.

[61] 'Exposure prone' is defined as 'where there is risk that injury to the worker may result in the exposure of the patient's open tissues to the blood of the worker', ibid, p.5; where the hands are inside the patient's body, cannot be fully seen, and there are sharp instruments or splinters of bone or teeth around - thus gloves are no protection.

confidentiality, there is evidence of the 1993 guidelines feeling a way forward from the 1981 position, influenced by criticisms such as those levelled by the 1990 internal inquiry in a hospital that had suffered an outbreak.[62] Recourse in difficult cases is offered to a UK Advisory Panel for health care workers infected with blood borne viruses, an extension of a panel which gave advice on HIV infected health workers; but at the date of writing this did not appear to include a hepatitis B expert.[63]

The 1993 guidelines offer a reassuring picture of the containability of hepatitis B in health care settings, stressing that with proper hygiene precautions the risk of transmission is very slight. But of course safety depends on the co-operation of health care workers. The dilemma is illustrated by the recent case of an 'e' antigen carrier surgeon who concealed his carrier status, until he was found to have transmitted hepatitis B to 19 patients. This doctor was condemned of causing a public nuisance and sent to prison for a year, under an interpretation of the law which was last used in 1815, against a woman who wheeled her smallpox-infected baby around the streets.[64] There seems evidence of a

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[62] Discussed above, pp. 223-4.

[63] UK Health Departments, 'Protecting health care workers', pp. 11, 17; the panel covered anaesthetics, dentistry, general practice, HIV disease, midwifery, nursing, obstetrics and gynaecology, occupational health, surgery, virology; future appointments will cover 'expertise on viral hepatitis and its epidemiology'.

[64] C. Elliott and C. Mihill, 'Prison for surgeon who carried hepatitis', Guardian, 30 Sept 1994; see also: R. Duce, 'Hepatitis doctor jailed for "terrible" deception', Times, 30 Sept 1994.

harsher response now than in the past, although this case was exceptional in that the doctor deliberately deceived his employers over his hepatitis B carrier status. In general, moves to publicise transmission from doctors to patients have been stepped up, both for AIDS and for hepatitis B, in the past two or three years.

Conclusions

This chapter has concentrated on health and safety issues around hepatitis B in the health setting, which figured most prominently on the policy agenda, initially allied with the perception of the disease as a hospital infection. During the 1970s, through the activities of health workers and hepatitis experts who were often themselves health professionals, hepatitis B was increasingly constructed as an occupational disease of health workers. Though hepatitis figured in other workplace settings such as prisons, there was little parallel concern about these workers.[65] Epidemiological evidence played only a relatively small part in such constructions: far more important were struggles over compensation and safety measures for laboratory workers, and health authorities' liability as employers versus their responsibilities to patients.

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[65] Though the workers themselves were concerned: letter from Assistant Secretary of Prison Officers' Association to ASTMS health and safety representative, on 'Viral Hepatitis/ Penal Establishments', 9 March 1983, followed by 'Case for extending the prescription of viral hepatitis as an industrial disease to prison officers' [typescript, 6pp.] I am grateful to Brian Gee for letting me see this; he was influential in drawing up the document: B. Gee, interview.

Different groups of workers had different agendas, for example laboratory technicians campaigned for compensation while dentists showed great concern over possibly infectious patients. But the resultant policy moves could have wider implications: in the case of the prescription of hepatitis B under industrial injuries legislation (1975), the ruling on 'close and frequent contact' with patients or blood thought to carry a risk of hepatitis B meant that not only laboratory workers, but many other categories of health workers, were covered. In the case of dentists' guidelines (1979), the expert group set down categories of patients regarded as risky, a listing that was to hold over into the vaccine era as we shall presently see.

There is no evidence of lobbying by surgeons to avoid screening, though that does not mean it did not occur behind the scenes: but in any case, professional solidarity of the experts with other medical professionals may largely explain the guidelines on hepatitis B and health workers (1981), which allowed carriers to continue working until and unless patients developed jaundice. Changes in guidance were probably brought about by a sequence of events: an outbreak in a London hospital in 1990, resulting in a thorough internal inquiry which called for review of the 1981 guidelines; a survey of surgery-associated outbreaks of hepatitis B conducted by the responsible CDSC officer, published in 1991; familiarity of several members of the expert advisory group with the case of Mr X, which showed that even a highly infectious carrier could conduct non-invasive surgery safely. When revised guidelines

were produced in 1993, none of this was mentioned and changes were predicated on notions around the 'e' antigen. This was hardly new;[66] what had altered in the last few years was visibility of the problem at the centre (in particular the CDSC) following noise at the periphery (in hospitals affected by outbreaks).

In Chapters 4 and 5 we saw safety measures against the spread of hepatitis B using the new antigen test in the areas of renal dialysis and the blood supply. In this chapter, the test has scarcely figured, until the refinement of testing for various antigens provided a means of identifying the most infective carriers. Instead, it appears almost as though a deal was negotiated, imposing strict safety precautions on health workers in return for allowing them to avoid screening. But health workers themselves pushed for preventive measures, while compulsory screening for all health workers was both too expensive and too controversial for the authorities to contemplate. Thus, to return to Muraskin's terminology, if the balance of individual rights (not to be screened) versus the public health interest (to know which workers are carriers) swung in favour of individual rights, it did so at the centre, for pragmatic reasons, not as a result of a conspiracy of health care workers. On the other hand, the various strands in this chapter demonstrate the power of professional interests to define strategies.

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[66] See Chapter 6, n. 20.

CHAPTER 8: VACCINE POLICY [1982-1993]

The introduction of a vaccine for hepatitis B in 1982 might be expected to spell the end of public health problems in relation to a disease which, though it affected relatively few people, caused considerable embarrassment to the DHSS from time to time. As this chapter will show, this was simply not the case; uptake of the vaccine was limited throughout the 1980s. Explanations can be offered using the literature on state interventions in the medical arena, and on the history of vaccination more specifically. The first part of the chapter looks at some of this literature, and considers how far hepatitis B in the UK fits these sorts of explanations and scenarios. It shows that a limited uptake of the vaccine, which followed central policy, cannot be explained simply by factors such as cost and demand. Other elements are important, such as commercial interests, people's trust in the safety of the vaccine, the devolution of responsibility for decisions on giving the vaccine to regional authorities, together with divisions within the medical profession over its applicability.

The second and third parts of the chapter trace debates and eventual changes in policy on the vaccine during the 1980s and into the 1990s. Several of the factors identified in relation to other vaccines can be seen to operate, with peculiarities due to the time and place: thus fear of the vaccine is related to fear of AIDS; high cost is particularly a problem when cost-cutting in the NHS is the rule of the day, and so on.

This story illustrates a number of themes that have recurred in this thesis: the lack of fit between policy and research findings (here, epidemiological evidence on main risk groups; evidence on the safety of the vaccine); and divisions between branches of the medical and health professions. Again, policy-making at the centre seems to follow, rather than lead, developments at the peripheries, despite the leading role of hepatitis experts in policy formation.

Background and context of vaccine policy debates

Success stories in terms of mass vaccination programmes have tended to involve viral diseases transmitted through droplet infection such as measles, diphtheria and polio. When Hollingsworth discusses vaccines as low-cost, high-demand new technologies, this is the range of diseases invoked, along with smallpox which is a rather different case, but likewise originally widespread.[1] By contrast, the incidence of acute cases of hepatitis B in the UK is low, with only a handful of deaths.[2] Similarly, carrier prevalence, under one per cent of the UK population, is low in global terms. When the first vaccine for hepatitis B was introduced in 1982, the high cost (over £60 a course) undoubtedly acted as a deterrent to widespread use, from the viewpoint of central policymakers. Potential recipients sometimes voiced a different reservation:

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[1] Hollingsworth et al, State intervention in medical care, p.125.

[2] S. Polakoff, 'Acute viral heptitis B reported to the Public Health Laboratory Service', Journal of Infection, 20 (1990), 163-8.

a fear of contamination of the vaccine, a fear that might have been overcome by a strong policy of vaccine promotion. Instead, a limited policy remained in place through most of the 1980s.

For the UK, hepatitis B vaccine appears as a high-cost, low-demand technology, so that the weak or restricted central policy of the 1980s seems unsurprising. But epidemiology and cost-benefit do not adequately explain policy. When a 1983 cost-benefit analysis favoured wider use of the vaccine for gay men, policy did not change. Yet in the 1990s, despite the background of a lower incidence, there are moves towards universal childhood vaccination against hepatitis B. The apparently 'pure' facts of epidemiology were constructed and reconstructed according to social forces, most immediately medical power relations.

Division of opinion on vaccination policy has a deep history, with the earliest clash perhaps falling within the general frame of 'individual liberty versus the public health'. In the nineteenth century, when smallpox vaccination became one of the first areas where state control was extended into the arena of individual health behaviour, public health medicine favoured compulsory vaccination, introduced in Britain in 1853. Anti-compulsory-vaccination alliances sprang up, involving some sections of the medical profession allied with other groups convinced on religious or philosophical grounds that the compulsory element should be removed. In a compromise solution, a conscience clause was introduced in

1898, but it has been argued that by this time the anti-vaccinationists had lost their ideological war, based on older Chadwickian ideals of public health as a sanitary and environmental exercise.[3] The newer preventive medicine sought to employ the tools of the bacteriological revolution, to attack each particular disease through destroying or neutralizing its causative agent. Retrospectively, doctors see the case for smallpox vaccination as totally vindicated by the worldwide eradication of smallpox, officially achieved by 1976 - an impressive victory for scientific preventive medicine.[4] Yet the sanitary and environmental approach looms large in the handling of problems presented by hepatitis B, both before the vaccine - the era of screening in the 1970s - and after the vaccine was introduced in the 1980s.

Immunization was to be a key weapon in the new preventive armoury of twentieth century public health medicine. However, its use was extremely variable, even when it seemed clearly possible to prevent huge numbers of deaths from infectious disease. As with smallpox vaccination, arguments about efficacy and possible complications could often be rallied on either side. In the case of diphtheria, Lewis has shown that Britain in the inter-war period had a much lower immunization

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[3] D. Porter and R. Porter, 'The politics of prevention: anti-vaccinationism and public health in nineteenth-century England', Medical History, 32 (1988), 231-52.

[4] H. J. Parish, Victory with vaccines. The story of immunization (Edinburgh: Livingstone, 1968); for more critical discussion on the role of variolation and vaccination in reducing smallpox mortality through a long run from the eighteenth century, see: P. Razzell, The conquest of smallpox (Firle, Sussex: Caliban Books, 1977)

rate than Canada despite its longer-established public health network, a situation only altered with the emergency situation of wartime.[5] Widespread use of diphtheria toxoid in Canada was favoured by unified medical opinion, a centrally orchestrated campaign, and a reliable supply of high quality, cheap toxoid. In Britain, with medical opinion divided and supplies available from disparate sources with less certainty of quality, the lack of a strong central policy was crucial - local health authorities were wary of supplying the toxoid lest they had to bear the cost. All of these factors, particularly the last, resonate with the case of hepatitis B vaccine in the 1980s. However, it should be noted that following wartime changes, immunization policy in general in Britain shifted to strong promotion of immunization for the common 'childhood' diseases, with the aim of achieving as near as possible universal childhood immunization.[6]

Hepatitis B seemingly presents a different set of problems from infectious diseases spread by droplet transmission, such as measles, diphtheria, whooping cough and polio. Transmitted by body fluids, it was regarded in this country mainly as an adult disease restricted to certain risk groups. As we have seen, the perception of which groups were most at risk changed over time, and did not necessarily fit the evidence, as health

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[5] J. Lewis, 'The prevention of diphtheria in Canada and Britain, 1914-1945', Journal of Social History, 20 (1986), 163-76.

[6] See successive issues of DHSS/Department of Health, Immunisation against infectious disease (London: HMSO). Measles, diphtheria, whooping cough and tetanus immunizations are given during the first year of life and polio at age five to most children; parents may opt their child out.

workers dominated the policy agenda. But in general, this pattern of acquisition of hepatitis B via blood, drugs or sex, mainly in adult life, is associated with a low or intermediate prevalence of the carrier state in the population, below five per cent.[7] That seemed to be the pattern for most of the developed countries.

But in many parts of the world hepatitis B is acquired in infancy and ten per cent or more may remain hepatitis B carriers, with an enhanced risk in adult life of liver disease including cancer.[8] For this reason, vaccine trials are being conducted in which hepatitis B vaccine is appended to the WHO extended programme of immunization for infants in areas of West Africa.[9] In south-east Asia, especially Japan and China, where primary liver cancer is a severe problem, widespread hepatitis B immunization has already been introduced, with low-cost vaccines produced in the region.[10] Thus, for both high prevalence countries and low prevalence countries, hepatitis B vaccination appears to have conformed with Hollingsworth's model: it diffused rapidly where there was a high demand and low cost, and vice versa.

But this high/low prevalence division in vaccine policy was

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[7] Zuckerman, Decade of viral hepatitis, pp. 7-23. The prevalence of markers of hepatitis B infection in the healthy blood donor population in the UK is low, at about 0.1-0.2 per cent, but this is thought to be an unrepresentative sample.

[8] London and Blumberg, 'Comments on role of epidemiology in investigation of hepatitis B'.

[9] Hall et al, 'Gambia Hepatitis Intervention Study'.

[10] Blumberg, interview, 5 March 1992.

apparently not a permanent fixture. With this sort of contemporary history, the situation can change before one's eyes. There have recently been moves towards hepatitis B immunization for all children in America, a lower prevalence country, and in Italy, an intermediate prevalence country.[11] This was a shift from a policy of selective immunization of risk groups, similar to the policy in the UK. There are now indications that the UK policy may soon change to universal hepatitis B vaccination, probably at puberty as with rubella immunization.[12] All through the 1980s there were calls for wider use of the vaccine in the UK, while central policy seemingly favoured the brake rather than the accelerator.

If the limited size of the perceived problem is one part of the explanation for a restricted UK response, the cost of the vaccine is another. With the price for a course of three doses over £60 through most of the 1980s, cost was clearly an issue for those deciding vaccine policy. The curious fact is that a vaccine was produced for use in Asia, in the mid-1980s, for around $1 a course.[13] Further study is required, of WHO input and the arrangements by which pharmaceutical companies are licensed to manufacture and sell their vaccines in different countries, in order to explain this remarkable price

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[11] On the US, Muraskin says: 'Universal vaccination for hepatitis B is now [1993] on the agenda at the CDC [Centers for Disease Control]': Muraskin, 'Hepatitis B as a model', p.130, n. 29; for Italy, see: S. Garattini, 'Italy: Compulsory hepatitis B vaccination' (Corr.), Lancet, 1991 (i), 228.

[12] 'Liver disease jabs "for all at 12"', The Guardian, 14 Oct 1991.

[13] Blumberg, interview, 22 Nov 1990.

differential which has been maintained over many years.

In addition to low prevalence of the disease and high cost of the vaccine, a third factor can be seen as inhibiting its deployment: consumer resistance. The vaccine available in the UK from 1982 onwards used as its raw material the plasma of donors with chronic hepatitis B. Rumours circulated that these donors included gay men. At the time when fear of AIDS was growing, but a test for HIV/AIDS in blood and blood products was not yet available, some of those to whom the vaccine was offered were unwilling to accept it. This appears to have been the case in fact even after an HIV test was introduced. A new genetically engineered vaccine which was marketed from 1987 proved more acceptable in the UK.

Dangers associated with immunization appear frequently in the history of other vaccines, and entered into the debate on their use. There could be a fear of pollution, associated with the source of vaccine material: cows, for smallpox vaccine; horses for diphtheria anti-toxin; gay men, for hepatitis B vaccine. Or there could be a fear of 'accidents' arising from a failure to modify or purify the vaccine sufficiently in manufacture: well-known instances occurred in the case of diphtheria and polio when live vaccine caused outbreaks of disease. Less well-known were deaths associated with measles convalescent serum, given to children in parts of Britain in 1937/8 - these deaths were later realized to have

been due to hepatitis B which contaminated the serum.[14] In the case of hepatitis B vaccine derived from human serum, fear of contamination was doubly present, both in terms of the hepatitis B virus (was it killed?) and the putative AIDS virus - and, some might argue, what other unknown dangers? - despite assurances, from the manufacturers and hepatitis experts, that dozens of careful steps in the preparation of the vaccine had unquestionably removed all noxious elements, and in particular, HIV.

Another issue arose in earlier debates, exemplified in the struggle over smallpox vaccination: the right of the individual to choose his or her own method to protect their health, versus the state's obligation to ensure the maximization of the public health. This would not at first glance appear relevant to the question of hepatitis B immunization, when the state was reluctant to offer the vaccine to any but a chosen few, and compulsory immunization was off the agenda. However, a similar theme emerges from the immediate prehistory of hepatitis B vaccination, as we have seen in the previous chapter, in debates around screening. For screening entails detection of carriers, and what Blumberg called 'a conflict between public health interests and individual liberty'.[15] In the UK during the 1970s, a compromise had been reached, between intervention in demarcated areas of especial danger (renal units, blood

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[14] MRC 2181/10g/2, record of informal meeting on 'Jaundice following administration of homologous serum', 13 Aug 1942.

[15] Blumberg, 'Bioethical questions related to hepatitis B antigen', 852.

laboratories), and reliance on individual responsibility elsewhere. The vaccine would be received into this pre-existing policy context, with established experts to advise on its application.

Policy and debate on the hepatitis B vaccine, 1982-1987

In the previous chapter we saw how a 1981 circular, based on advice from the Advisory Group on Hepatitis, addressed the problem of hepatitis B carriers among NHS staff: or rather, skirted around it. Then in 1982, the first hepatitis B vaccine was given a UK licence; this was a plasma-derived vaccine, manufactured by Merck Sharp and Dohme. DHSS guidelines were issued in October 1982, offering advice on the new vaccine.[16] They pointed out that the vaccine would only be available in very limited quantities initially, that it was expensive and that NHS resources were stretched. The circular stressed that hepatitis B occurred at a low rate in the UK, with only about 1000 overt cases a year, although the risk of becoming a chronic carrier from asymptomatic infection was mentioned. These provisos set the tone for restricted recommendations on vaccine use, reasonable enough when supplies were limited. However, while the guidelines remained in place essentially unaltered until 1988, supplies rapidly expanded, and during the mid-1980s the rate of acute hepatitis

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[16] DHSS circular CMO(82)13/CNO(82)11, from Henry Yellowlees, Chief Medical Officer and Mrs A. A. B. Poole, Chief Nursing Officer, to General Medical Practitioners, District Medical Officers and District Nursing Officers, 15 October 1982, on 'Hepatitis B vaccine: guidance on use', letter with 2pp. attachment.

B increased to 2000 a year, before falling back to previous levels.[17] This increase in the disease after introduction of a vaccine constitutes a paradox, undermining vaccine policy.

The 1982 vaccine guidelines concentrated on two major categories: (i) health service staff and (ii) patients and family contacts. Staff in mental handicap institutions were prioritized, as were those in contact with known carriers or haemophiliacs - though prioritization by no means meant the vaccine was actually delivered. Other than these categories, the guidelines mention laboratory workers handling infected material, and staff sent abroad to areas of high hepatitis B prevalence. Patients entering mental institutions, renal dialysis patients, and spouses or other sexual contacts of known carriers were also priorities. The list does not include surgeons, dentists or nurses, nor does it mention 'lifestyle' risk groups such as gay men and drug users. The closest precedent seems to be the list of high-risk groups mentioned in the report on hepatitis in dentistry:[18] this is logical, given that the dental group had been amalgamated into the Advisory Group on Hepatitis.

Through the 1980s, there was pressure for the extension of the hepatitis B guidelines to include more occupational and 'lifestyle' groups. For those who wanted the vaccine to be made generally available to the group they belonged to, or to

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[17] Polakoff, 'Acute hepatitis reported to PHLS', graph, 164.

[18] DHSS, Hepatitis in Dentistry, p. 2.

client groups, the guidelines appeared restrictive.[19] They were open to a degree of interpretation by health authorities, but judgement of particular doctors in particular cases was the chief arbiter. Since there was no item of service payment attached to the vaccination, a persuasive case had to be made by individual doctors wishing to use the vaccine more widely.[20]

One member of the Advisory Group on Hepatitis with a global perspective on the problem, Zuckerman, published regularly on vaccination policy. In 1982, six months before the DHSS guidelines came out, Zuckerman wrote on the priorities for hepatitis B immunization in the British Medical Journal - mentioning for Britain the categories selected by the DHSS but more specifically on the patient care side:

> ... medical and laboratory staff of hepatitis reference centres and staff engaged in the development and production of hepatitis B vaccine; staff of liver units and gastrointestinal units with an interest in the liver; staff of surgical intensive care units; dental surgeons, dental nurses, and ancillary staff of units where dental care is provided for known hepatitis B carriers ...[21]

These were subsumed in the 1982 guidelines under the rubric of 'personnel directly involved in patient care over a period of time, working in units giving treatment to known carriers of

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[19] Anonymous informant in touch with many such groups, interview, 12 July 1991.

[20] Across the country, doctors' ability to use the vaccine varied according to the line taken by their local Family Practitioner Committee (FPC); see for example Cheshire FPC standing by its policy of paying item of service fees for hepatitis B vaccinations in the face of DHSS oppposition: 'FPC stands firm on hep B fee policy', General Practitioner, 3 April 1987, p. 10.

[21] A. J. Zuckerman, 'Priorities for immunisation against hepatitis B', British Medical Journal, 284 (1982), 686.

hepatitis B infection'. However, there was good reason for dentists in normal practice as well as those in special units to wish for vaccination, and some would argue, for their ancillary staff as well. Otherwise, Zuckerman's list pinpoints those working closest to the 'coal face' in research or clinical settings likely to involve contact with the hepatitis B virus.

In the same article, Zuckerman introduced a group which was not subsequently covered in the DHSS guidelines in October:

> Male homosexuals are another group at high-risk of hepatitis B and an important reservoir for transmission of infection because of their considerable promiscuity.[22]

At this time - mid to late 1982 - AIDS was only just beginning to be recognized, and few major studies of 'gay lifestyle' linked with the new disease had appeared.[23] But the first recognition of the higher risk of hepatitis B associated with male homosexual behaviour had been published in the UK in 1973,[24] followed in 1975 by a large US study.[25] Appreciation of the link had gradually grown in the UK, especially amongst those working in inner London genito-urinary medicine clinics with a high proportion of homosexual men among their clients,

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[22] Ibid, 687.

[23] For a discussion and evaluation of papers in this field see: Oppenheimer, 'In the eye of the storm', section on 'The "life-style" hypothesis: experimental work', pp. 275-80.

[24] Fulford, Dane et al, 'Australia antigen and antibody among patients attending a clinic'. This and another paper mentioned in Chapter 6, n. 6, substantiate Dane's claim of a British 'first' for recognition of sexual transmission.

[25] Szmuness, Much et al, 'On sexual behaviour in the spread of hepatitis B'.

but it was not widely accepted for some while.[26]

Awareness grew among gay men themselves, possibly ahead of many in the medical profession, that a new disease had been added to the spectrum of sexually transmitted diseases: unusual in that it was untreatable. As on the American West Coast, so also in London, the gay community learned about hepatitis B through the 1970s. In 1982, a number of gay men in London formed a group for chronic hepatitis B sufferers - those who had failed to clear the antigen, and therefore remained infectious - calling themselves 'Groups B'.[27] Some had been advised by their doctors to abstain from sex and alcohol, but received little other advice. Others had found difficulty in obtaining information on long-term prognosis, and implications for employment. One of the group's aims was to exchange information. Another aim of Group B was mutual support, in view of stigmatization and difficulties associated with carrier status. A third aim in the early days was social interaction with other gay men who, as hepatitis B carriers, would not be at risk if a sexual relationship ensued: this aspect was particularly encouraged by some doctors. But the common ground of sharing the same disease proved to be rather a party killer, especially when the ban on alcohol was taken seriously. With the growing recognition of AIDS, this social

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[26] Doubt was thrown on this link by colleagues in the blood transfusion field: 'I raised it at meeting after meeting and they said I was obsessed by sex': Barbara, interview. A CDSC reference virologist decided not to publish her survey of hepatitis B patients because she could not understand why so many were single men: Vandervelde, interview.

[27] Group B, interview, 12 May 1991. The remaining points in this paragraph are based on this group interview.

function rapidly tailed away.

For the homosexual group who were already carriers of hepatitis B, vaccination was not a solution, excepting as a protection for a steady partner in some cases.[28] But there were arguments for promoting widespread screening and vaccination among the gay community, expressed perhaps most succinctly in a 1983 article by Adler and others on the costs and benefits involved.[29] Even without considering the costs of chronic sequelae of hepatitis B carriage - in other words only looking at the acute form of the disease - Adler's group from the Middlesex genito-urinary medicine department concluded that offering vaccination to homosexuals could save the national economy several million pounds a year. Their point was not taken up by the DHSS for some time to come, although Zuckerman in 1984 again included 'promiscuous male homosexuals' in his list of target groups for immunization.[30]

In fact, this 1984 article is instructive as a marker in the development of opinion with regard to hepatitis B vaccination, bearing in mind that the author was a dominant figure in both British government and WHO policy making. With no reference to the 1982 DHSS guidelines on hepatitis B vaccination,

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[28] An alternative solution was interferon treatment, tried on hepatitis B carriers including several members of Group B in the early 1980s with low success rates: according to Group B this experimental treatment caused daunting side-effects.

[29] M. Adler, R. M. Belsey et al, 'Should homosexuals be vaccinated against hepatitis B virus? Cost and benefit assessment', British Medical Journal, 286 (1983), 1621-4.

[30] A. J. Zuckerman, 'Who should be immunised against hepatitis B?', British Medical Journal, 289 (1984), 1243-4.

Zuckerman listed six main groups to be targetted in Britain: (i) detailed categories of health care personnel; (ii) mental institution, haemophilia, renal and certain surgical patients; (iii) sexual partners of hepatitis B patients; (iv) infants of carrier mothers; (v) immigrants or refugees from high prevalence areas such as South East Asia, promiscuous homosexuals, prostitutes and narcotic drug abusers; (vi) 'lower risk' groups such as long term prisoners, prison staff, ambulance and rescue service workers, and selected police personnel.[31] The fifth, rag-bag group includes those at risk because of country of origin, sexual behaviour and drug-injecting. Perhaps in drawing attention to these groups, Zuckerman was testing the climate of opinion among the medical profession, for a possibly controversial expansion of the vaccination programme. Although he claims to have found the DHSS co-operative,[32] there was no sign of their willingness to revise the vaccination guidelines at this point.

Besides expansion of the immunization programme, Zuckerman expressed a second strong theme: a counterattack against all those who expressed doubts about the safety of the plasma-derived hepatitis B vaccine. Arguments against the vaccine were 'emotional, vociferous, and indeed irrational'.[33] This outburst followed a meeting at which Sheila McKechnie, ASTMS safety officer, annoyed Zuckerman by stating that she would

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[31] Terms are those used in original article; numbers have been added by present author.

[32] Zuckerman, interview.

[33] Zuckerman, 'Who should be immunised?', 1243.

not recommend the vaccine for her members (including many laboratory workers) in the light of its possible association with AIDS. To reinforce the evidence on the safety of the vaccine, Zuckerman used the analogy of hepatitis B specific immunoglobulin - also prepared from pooled plasma - which he claimed was delivered to 20 million recipients in one four-year period without mishap.[34]

The pharmaceutical company which marketed the plasma-derived hepatitis B vaccine in this country, Merck Sharp and Dohme, undertook an active campaign to increase support for the vaccine in the medical and nursing professions. Some sectors were more favourably inclined than others: notably dentists, and opinion formers in the nursing profession. The Royal College of Nursing (RCN) expressed willingness to advocate vaccination for all nurses as early as 1982, when RCN Labour Relations Officer John Goodlad 'forcefully declared that "there is nowhere near enough [vaccine] to meet the urgent need of nurses"' for hepatitis B vaccination, while Assistant Nurse Adviser for the RCN Society of Psychiatric Nursing Robert Macrowan called for nurses working with mentally handicapped patients to receive priority, because bodily contact, bites and scratches from patients and 'immense problems of staff shortages' made them the highest risk group among health professionals.[35] But the RCN still had to convince the bulk of their members, as well as to secure

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[34] Ibid.

[35] 'New campaign for hepatitis vaccine', Nursing Standard, 19 Aug 1982.

health authority interest.

Persuasion was conducted by a combination of agencies, through the nursing press, conferences and publications. In November 1984, the LSHTM Department of Community Health hosted a conference on 'Hepatitis B - who should be immunised?'. Three hundred doctors, nurses, trade union representatives, medical technicians and students attended, to hear Professor Zuckerman emphasise the safety of the vaccine, and Roger Williams of King's College Hospital Liver Unit advocate immunization of all health staff.[36] In 1986 a conference on nursing and hepatitis B in the UK supported by Merck Sharp and Dohme attracted over seven hundred nurses - so many that the organisers had to change the venue at the last moment to the Wembley Conference Centre.[37] But despite the efforts of Zuckerman and colleagues such as Elizabeth Fagan of King's Liver Unit who pronounced the vaccine 'deader than dead than dead', the 'dangerous vaccine' label stuck, for some groups at least, until it was withdrawn from sale.[38]

For a clear illustration of the resistance to hepatitis B vaccine, we can turn to a publication from the 1986 conference, featuring articles by leading British names in the field, with an underlying theme of the need for more

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[36] 'At risk of hepatitis B', Nursing Standard, 22 Nov 1984.

[37] Anonymous informant, interview.

[38] Ibid. Fagan possibly borrowed the quote from Zuckerman; see: RCN Safety Representatives Conference Co-ordinating Committee, 'Hepatitis B and nursing in the UK. Report from the Wembley Conference', April 1987. The plasma-derived vaccine was withdrawn in 1988.

widespread vaccination.[39] One report in this booklet, from a London hospital, described the sort of risks run by staff:

> ... we are specially concerned about the risks of hepatitis B because the hospital is situated in a part of Central London where there are many male homosexual patients in the community and increasing numbers of drug addicts. Many of these have hepatitis B and present to our casualty department, often with various kinds of trauma problems, road traffic accidents and so on. Indeed we have had the problem once of having had admitted to us an unconscious patient who retrospectively was found to be incubating hepatitis B and had undergone major surgery and caused an outbreak of hepatitis B in our operating theatre and intensive care unit staff.[40]

Between 1983 when the hospital bought 100 courses of the vaccine, and 1986 when the microbiology department undertook a survey, only ten members of staff had taken up the vaccine. Interest was high in the intensive care unit and higher still in the accident and emergency unit, no doubt as a result of the previous outbreak. Staff on the AIDS ward were not interested, despite education:

> The reason is probably that these staff are demoralised at seeing young men die so frequently. The fear of AIDS has terrified them, and even though we have reassured them these staff still at the moment are not accepting the vaccine easily.[41]

The fear of AIDS transmission was the commonest reason for refusal to accept the vaccine among all staff; but many had not previously been aware it was available. And of the staff circulated with the vaccine questionnaire (240 nurses and 124 doctors), a high proportion of nurses replied but only 20 per

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[39] R. Short and G. Jones (eds), Hepatitis B in the UK, proceedings of a conference at the Royal Society of Medicine, Oct 14 1986 [48-page publication sponsored by Merck, Sharp and Dohme] (London, 1986)

[40] D. Shanson, 'Attitudes of staff [to] vaccination in a London hospital', in Short and Jones, Hepatitis B in UK, p. 42.

[41] Ibid, p. 43.

cent of the doctors.[42]

Some sections of the medical profession were more willing to press for extended coverage: where hospital doctors held back, pathologists, and those in charge of clinical laboratories, were more likely to promote vaccination. In the first half of 1987 there was a further flurry of activity on the pages of the British Medical Journal about hepatitis B vaccination. Roger Finch, senior microbiologist at Nottingham City Hospital and University, kicked off with a leading article calling for promotion of hepatitis B vaccination.[43] He argued that it was not just a matter of categories, but that there should be active efforts to offer the vaccine to target groups in the health service and in the community, given poor uptake rates to date. Both the high cost of the vaccine and fears about transmission of AIDS had hampered delivery, but Finch felt these could be countered. He reiterated the pro-vaccine lobby's view that the vaccine was proven beyond doubt to be safe. As for costs of immunization, these should be offset against those of chronic hepatitis B, immunoglobulin for needlestick injuries, and compensation under the Industrial Injuries Act.[44] Finch also mentioned the study by Adler's group, indicating cost-effectiveness for hepatitis B vaccination of homosexual men, a group which Finch felt could

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[42] Ibid, p. 42.

[43] R. G. Finch, 'Time for action on hepatitis B immunisation', British Medical Journal, 294 (1987), 197-8.

[44] Finch gave no figures for sums awarded in compensation; my enquiries at the National Audit Office have so far failed to bear fruit but the search continues.

more readily be reached than drug users, though he suggested logistics for both groups.

Argument in the correspondence pages over several aspects of Finch's case centred on health care workers, especially the cost-effectiveness of immunizing all 400,000 nurses in the NHS with a vaccine then costing £63.50 for a course of three injections.[45] A pertinent case was put for immunizing medical and nursing students against hepatitis B.[46] Sheila Polakoff, now in charge of a Hepatitis Epidemiology Unit at the CDSC, and Professor Zuckerman aired their differing interpretations of figures on acute cases and estimates for chronic cases.[47] Misunderstanding about the source of vaccine supplies was corrected.[48] In all, this debate and correspondance lasted from January to June of 1987. By raising the profile of hepatitis B vaccine in the medical press, it may have strengthened the hand of those who were campaigning behind the scenes for greater governmental promotion of the vaccine.

Policy and debate on the vaccine, 1987-1993

A year later, in July 1988, revised guidelines on hepatitis B vaccine were included in a DHSS circular offering further

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[45] Correspondence, British Medical Journal, 294 (1987), 509 (Malcolm S. Gatley); 771 (Arie J. Zuckerman); 975 (J. K. Anand).

[46] Ibid, 841 (Mr Perry Board).

[47] Ibid, 771 (Zuckerman); 1031 (S. Polakoff, Hepatitis Epidemiology Unit; E. M. Vandervelde et al, Virus Reference Laboratory; both Central Public Health Laboratory Service).

[48] Ibid, 1232 (M.P. Shoolman); 1615 (S. Polakoff).

recommendations on vaccination. Each district health authority had been asked, in 1985, to appoint an immunization co-ordinator, with the aim of improving overall uptake of vaccines. This co-ordinator was now required to deal with the new measles, mumps and rubella combined vaccine, but they were not asked to add hepatitis B to the childhood immunization programme. For hepatitis B vaccine, the focus remained on health staff, with health authorities bearing responsibility for deciding the order of priority among their employees. Voluntary workers with drug misusers 'should also be considered'. Among patients, the Chief Medical Officer drew attention to two 'lifestyle' groups: 'individuals who frequently change sexual partners' and 'injecting drug misusers'. He suggested that counselling about HIV risks could be offered along with hepatitis B immunization to these clients.[49]

This advice, subsumed in a circular dealing mainly with childhood vaccinations, was probably slow to have much impact, either in relation to sexual transmission, or drugs use. While the 1988 circular referred to 'individuals who frequently change sexual partners', concern centred on male homosexuals. A 1989 study revealed lack of screening or immunization of gay men attending genito-urinary medicine clinics.[50] A London clinic at the heart of the recognition that homosexuals were

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[49] DHSS EL(88)P/125, from R. L. Cunningham of Child, Maternity and Prevention Branch to Regional and District General Managers, etc., on 'Immunisation', July 1988.

[50] R. Loke, I. Murray-Lyon et al, 'Screening for hepatitis B and vaccination of homosexual men', British Medical Journal, 298 (1989), 234.

at high risk of hepatitis B reported a similar finding, about itself, in 1991.[51]

A tale from an Edinburgh community physician is illuminating on attitudes to drug injectors as clients for vaccination:

> The epidemic here in about '84 was very considerable, the hep B epidemic in drug users, and I remember going to see my boss and saying: "Do you think we ought to vaccinate drug users?", and my boss, who was a very level-headed and sensible chap, said: "You must be absolutely bloody crazy!" You know, if you're thinking of using this vaccine which was £120 a course on a group where you won't even [be able to maintain contact], he was quite right, quite apart from the benefit of it, you'd probably not get your three doses into them, you'd waste half of it.
> - So was he doing a sort of cost-benefit analysis?
> - Well, I mean, yes, on the back of an envelope.[52]

This informant calculated that, following the outbreak of heroin injecting in Edinburgh in the early 1980s, over 90 per cent of drug-users in the city would have been infected with hepatitis B; of these, about 10 per cent probably became carriers who might be infectious.[53] Nowhere in the UK was there a concerted policy of seeking out sexual partners of hepatitis B carriers for vaccination. But the problem had since been overshadowed by the AIDS epidemic - in Edinburgh, retropective testing of blood samples from drug injectors with hepatitis B showed most seroconverted for HIV.[54]

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[51] N. Bhatti, R. J. C. Gilson et al, 'Failure to deliver hepatitis B vaccine: confessions from a genitourinary medicine clinic', British Medical Journal, 303 (1991), 97-101.

[52] G. Bath, interview, 20 Aug 1991.

[53] Ibid; see also: G. Bath and R. A. Carson, Hepatitis B notifications in Edinburgh - a study by Edinburgh District Council and Lothian Health Board (Typescript, 33pp., Feb 1986)

[54] Robertson, 'Edinburgh epidemic'.

A study of hepatitis B screening and vaccination in NHS drug treatment facilities, published in 1990, showed that about two-thirds did not screen or offer vaccination. However, half thought that partners of hepatitis B clients should be vaccinated, and two-thirds would recommend vaccination for drug users who continued to share needles.[55] As a national needle exchange scheme had been introduced in 1987, because of the AIDS epidemic, hepatitis B immunization for drug users may have been less urgent than in the early 1980s. As mentioned earlier, figures for acute hepatitis B in the UK show a clear peak in 1984 (about 2000) followed by a rapid drop back to previous levels (below 1000 per annum).[56] The reasons for the fall are less obvious than those for the rise, but may be associated with containment of spread by the sexual route in the light of HIV, rather than dramatic changes in drug injecting behaviour.

A story from the 1990s returns us to Muraskin's work on the conflict between individual rights and public health. At an infant school in Huddersfield, on the first day of term following the Easter holidays in 1991, parents of about a third of the 193 pupils kept their children at home, in protest against the arrival of a new pupil, a seven year old boy who was a hepatitis B carrier. The parents were not arguing for exclusion of the carrier boy, but said they wanted

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[55] M. Farrell, M. Battersby and J. Strang, 'Screening for hepatitis B and vaccination of injecting drug users in NHS drug treatment services', British Journal of Addiction, 85 (1990), 1657-9.

[56] See p. 247.

their children to be immunized before they would allow them back to school. Kirklees council, the responsible authority, offered reassurance: 'medical advice is that the risk of the virus being passed on is minimal and vaccinations are unnecessary'.[57] As the boycott continued, the Health Secretary, William Waldegrave, speaking in the House of Commons, urged the 'misguided parents' to end their protest. The parents were looking for a retired teacher to help them set up an alternative school.[58] After a few days the situation was resolved by a visit to the parents from Dr Judith Hilton, Senior Medical Officer responsible for hepatitis B in the Medical Division at the DoH, and Dr Julia Heptonstall, in charge of hepatitis B surveillance at the CDSC.[59] That two such high-ranking officers should be sent to convince parents that there was no need for their children to be vaccinated, even in the presence of a hepatitis B carrier, indicates strong concern at the DoH to avoid mass hepatitis B vaccination.

Yet, later in 1991, there were hints of a change in policy: even, as mentioned earlier, towards universal childhood vaccination.[60] There was no immediate action, however. In 1992, the MRC funded a study to examine hepatitis B vaccination policy in the UK, with the aim of finding out how

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[57] 'Children kept out of school in protest over virus carrier', The Times, 16 April 1991.

[58] 'Hepatitis boycott goes on', Morning Star, 19 April 1991.

[59] Hilton, interview.

[60] 'Liver disease jabs "for all at 12"'.

current policy actually operates 'on the ground', and undertaking cost-benefit analyses of various projected policies for the future.[61] One of the few previous largescale cost-benefit studies, which looked at health staff in Northern Ireland in 1988, had concluded that the costs of hepatitis B vaccination for all health staff outweighed the benefits.[62] The current MRC study appears to have a much wider brief, perhaps coming closer than most of the research surveyed in this study to exemplifying policy-stimulated research.[63] It was taking place in an atmosphere where universal childhood vaccination was under consideration, but would represent an about-turn for UK policy.[64]

Meanwhile, it appears that health authorities were already expanding their programme of immunization for certain groups of staff, especially those in mental health institutions, in the light of changes to safety legislation and especially the removal of Crown Immunity in 1991. This response was probably hastened by the death from hepatitis B of a mental health nurse who had been bitten by a patient, a case which the RCN

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[61] P. Mangtani, personal communication, 14 Oct 1992.

[62] McKee, 'Hepatitis B in Northern Ireland - who should be immunised?'.

[63] This in no way implies that the outcome of the research was pre-determined; two papers from the study will shortly be published but were still confidential as of Dec 1994.

[64] This thesis was constantly overtaken by events during drafting, with one informant confidently predicting universal hepatitis B vaccination in the UK within two years: A. Hall, personal communication, passing on staircase at LSHTM, 30 June 1993.

planned to take to court.[65] Health authorities around the country must have been alerted by the implications. Then in 1993, after a number of cases in which patients were infected with hepatitis B by carrier surgeons, the DoH moved towards hepatitis B screening for about 100,000 staff involved in surgery and other invasive procedures.[66] Doctors, concerned that this might be a first step towards compulsory HIV testing, opposed the move. A year and a half later, the BMA voiced opposition to a new policy of screening prospective medical students for hepatitis B.[67] It seems a probable expansion of immunization is being preluded by an expansion of screening.

Conclusions

This chapter looked at policy on hepatitis B vaccine in the 1980s and into the 1990s, and argued that factors identified in this case are shared with other vaccine histories and perhaps with public health policy more generally. While 'rational' facts established by research, such as the epidemiology or potency of a disease, may seem to point the way towards policy, they are often not the chief determinants of policy. The pattern of transmission of hepatitis B, like many diseases, has remained fairly constant while policy has

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[65] S. Brewer, interview, 14 Dec 1992; the outcome was uncertain at that date.

[66] 'NHS staff to be tested for hepatitis B', The Independent, 11 June 1993.

[67] O. Wojtas, 'Hepatitis B screening queried', Times Higher Education Supplement, 8 July 1994.

changed over time and appears likely to change even more substantially in the future. It is important to recognize, too, that features of a disease that appear to the experts as hard 'facts' are the constructs of a given moment.

The chapter analysed the reasons for, and development of, a limited policy, that avoided active promotion of widespread vaccination. Although vaccine policy was directed by the DHSS/DoH, and analysed mainly at this level, it was implemented by regional health authorities. As with other historical examples, the delegation of final responsibility for decisions about who should receive the vaccine, from the centre to the peripheries, acted as a very effective brake on wider uptake of the vaccine.[68] At every level, health officials sought advice from medical experts who acted as 'gatekeepers' or arbiters, but (again, with historical parallels) this medical opinion was often divided and unable to push very strongly in one direction.

There appears to have been a divide between clinicians and laboratory doctors, with the latter more willing to advocate wider use of the vaccine. Dentists promoted the vaccine, surgeons often resisted it. Among nurses there was a widespread campaign, with enthusiastic leadership from opinion formers, which created a high profile in the nursing press: response from the rank and file was uneven. Ideas about which

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[68] Compare Halper's analysis of cost containment in the case of kidney dialysis, where a similar brake mechanism is identified for the early years: T. Halper, 'Life and death in a welfare state; end-stage renal disease in the United Kingdom', Milbank Memorial Fund Quarterly, 63 (1985), 52-93.

categories of nurses and technicians should be prioritized for vaccination often departed from those indicated by apparent risk: groups which felt they were more at risk, and campaigned most strongly, were most likely to receive priority.[69]

On the supply side, the pharmaceutical companies which manufactured and distributed the vaccine conducted a persistent campaign to promote their product. They attempted to overcome the image problem of the first vaccine with the support of scientific evidence: there is some indication of success with dentists and nurses but less with technicians, who were however a smaller client group than nurses. When a different company brought out the genetically engineered vaccine, they had the advantage of the ground having been broken, their image was safer, and their price was lower. It is perhaps surprising, then, that a year elapsed before a change in vaccine policy, and several more years before distribution to NHS employees was stepped up.[70] Promotion among the much larger risk groups 'in the community' (gay men, IVDUs) lagged still further.

The analysis offered in this chapter shows how history helps to explain the apparent inconsistencies and vagaries of recent

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[69] Thus operating theatre nurses, who were not at most risk but thought they were, tended to be prioritized; similarly dental nurses; while mental health institution nurses and laboratory technicians lagged behind.

[70] A sign of continuing campaigning by the producer may be an undated, but recent, quasi-journal, Viral hepatitis, (subtitled Action on hepatitis B as an occupational hazard), produced by the Viral Hepatitis Prevention Board 'under the auspices of the Society of Occupational Medicine', supported by 'an educational grant' from Smith Kline and Beecham.

health policy.[71] In the cases of smallpox and diphtheria, lay and medical opinion about the advisability of vaccination was deeply divided: so it was with hepatitis B. The epidemiology and natural history of hepatitis B, built up by multiple research findings, was open to different interpretations. During the 1970s, in the 'pre-vaccine' era, hepatitis B was constructed chiefly as an occupational disease of health workers. The nature of the work itself came to define the risk, rather than a particular incident. The risk of a health worker infecting a patient was seen as extremely rare. Screening all health workers and weeding out carriers was avoided: there might be too many, and especially too many among the higher status groups such as surgeons. The unknown chance of transmission was outweighed by the known distress, stigma and probable loss of livelihood for those found to be carriers. In the balance of individual rights versus public health interests, at this stage there seemed good reason to favour individual rights.

Although the terms of the balance would seem to have altered completely with the advent of the vaccine in 1982, pre-vaccine policy continued to permeate thinking through the 1980s.[72] It could have been argued - and was by vaccine advocates - that

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[71] Of course this is not news. In the related field of AIDS history, see for example: R. Porter, 'History says no to the policeman's response to AIDS', British Medical Journal, 293 (December 1986), 20-27; Fee and Fox, AIDS: burdens of history; Berridge and Strong, 'AIDS and relevance of history'.

[72] One anonymous commentator asserted that policy on screening changed with the advent of the vaccine which gave screening a public health benefit outweighing individual objections; while logical, this sequence is not supported by my evidence and analysis.

it was in both the individual's and the public health interest to initiate widespread screening and vaccination. But the centrality of health workers who had been spared screening and were now the chief targets of vaccine policy kept individual rights, to avoid screening, at the forefront of the agenda. Compulsory and universal screening for health workers would benefit those who had not yet been exposed to the disease and could be protected by the vaccine, but it would expose those who were carriers, for whom the vaccine was no solution whatsoever.

Divisions over screening and vaccination, leading to a limited vaccine policy, suited the economizing inclinations of the DHSS/DoH through a period of increasingly stringent cost-cutting health policy. Cost appears as a dominant factor inhibiting promotion of the vaccine, until other potent factors showed that it might be overridden.[73] From the mid-80s, there was the AIDS debate: changes which were introduced because of AIDS could spill over to affect hepatitis B - for example, needle exchange schemes for IVDUs - gradually drawing groups other than health workers towards the focus of the policy gaze. Then, changes in the law, affecting the liability of health authorities as employers, meant that it became potentially expensive to fail to vaccinate employees. Meanwhile, international health bodies and other countries, including some with moderate rates of hepatitis B, advocated wider vaccination. These pressures together probably explain why universal childhood hepatitis B vaccination is now under

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[73] Or perceptions/calculations of cost may have altered.

consideration as a viable option in the UK.

Perhaps it is dangerous to say that the test of an analysis or hypothesis is its predictive value, but on the basis of the argument for a link between policies on screening and those on vaccination, it could be predicted that the move towards compulsory hepatitis B screening for hospital doctors indicates the likelihood of similar HIV screening, to be followed by a much stronger policy on the AIDS vaccine, if it should be developed. The other lesson is that universal vaccination cannot be counted as likely, if an AIDS vaccine costs as much as the hepatitis B vaccine: it is even less likely for those poorer countries where prevalence is far higher.[74]

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[74] Low cost hepatitis B vaccines available for poorer countries have been widely used in parts of Asia, as indicated, but not in many African countries where even a cheap vaccine consumes a large proportion of the annual health budget per person.

CHAPTER 9: CONCLUSIONS

The purpose of this chapter is to draw out themes from the thesis, related to the aim set out in the Introduction: to throw light on the relationship between medical research and health policy, in the case of hepatitis B in the past fifty years. Minor points that have been included in conclusions to each chapter will not be reiterated here; and for an outline of the narrative, readers are referred back to the Introduction.

The main section of this concluding chapter opens with definitions of policy that informed the study, and discusses the lack of fit between science and policy which was observed from the outset. A summary will be given of the main policy inputs and outputs that have been traced for hepatitis B. Second, constructions of the disease will be analysed, enabling policy to be related to changing perceptions of risk and notions of crisis. A sub-theme here is the frequent emergence of hepatitis B as a hazard associated with medical innovations. A third major theme concerns research networks, arising from contacts between researchers at different levels; these will be shown to overlap with policy networks. This links with notions of desired and undesired inputs, which seem to operate in the filtering of advice by central authorities. Fourth, a central-local dynamic which was identified in several areas of policy will be examined, showing that policies often originate from the peripheries rather than the centre. Fifth, the idea of the 'importance of not knowing' -

an anthropological concept - will be applied to not knowing which doctors or patients were carriers. There will be discussion of the idea that the low profile of hepatitis B in the public media, compared to that of AIDS, was connected with health workers' anxieties over publicity.

A separate section makes comparisons between the policy history of hepatitis B and that of AIDS, beginning with an alternative explanation for the different media profiles of the two diseases. Continuities as well as contrasts can be observed in the pattern of advisers drawn into policy making, while parallels can be seen in debates over who should be screened and the use of the test. Muraskin's arguments on individual rights versus the public health interest are especially relevant here. It is also interesting to compare the use of history in debates around the two diseases. Both from this and from the previous section, ideas about topics for further research are generated: these will be briefly discussed in the penultimate section. In the final remarks, the strongest findings and themes will be underlined again.

General discussion

The idea of looking at the relationship of research and policy arose in the early stages of this project, when initial contacts pointed towards researchers as key players in the policy arena. A survey of literature from policy science and the history of health policy suggested that it was unsafe to rely on a model of policy-makers prompting research on areas

of concern to them, and of research findings then feeding directly into policy (the 'rationalist' model of the relationship). It soon became obvious that this was not what had happened in the case of hepatitis B. There was a striking lack of fit between research findings on the epidemiology of the disease and policies on screening and vaccination. The use of the two major technologies resulting from research could not be understood simply as 'application' of that research.

A much more fluid model of policy making, in which research was utilised very selectively, had to be employed; and determinants other than the supposedly rational ones of science had to be sought out. Of course there is an argument that a lack of fit between science and policy is a good thing.[1] In an alternative model, research diffuses gradually through networks or policy communities. These networks will be discussed presently.

This seems an appropriate point to present in summary form the inputs that seem to have carried weight in the case of hepatitis B, given that science was not the dominant input. It will also be useful to summarise policy outputs, in terms of reports and guidelines, to inform the subsequent discussion.

Three important types of input - that is, factors which

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[1] Collingridge and Reeve, Science speaks to power, especially Ch. 1: 'Science and policy - an unhappy marriage', pp. 1-6.

stirred action in the central policy and decision making machinery of the Department of Health - can be identified:
(1) Acute outbreaks - for example among troops receiving yellow fever vaccine in 1942/3, or in renal dialysis units in 1965-72 - called forth strong and definite measures, beginning with the establishment of committees.
(2) Sporadic cases of acute hepatitis B in a health service setting caused concern, perhaps depending on the overall numbers. Post-transfusion hepatitis received most attention.
(3) Other instances of 'noise' from concerned groups (e.g. laboratory technicians) or embarrassment (as in the case of dentists turning away suspected carriers) also stirred a response in terms of policy. Groups further away from the mainstream health forums, such as prison officers or mental health institution nurses, were less likely to be heard. Groups altogether outside the health setting received very little policy attention.

Main policy outputs have been identified as follows:
(1) During the war, centrally coordinated research led to policies to reduce transmission in venereal disease clinics and in the blood supply (probably ineffective in the latter case).
(2) Following the Australia antigen finding, central advice was issued on the use of antigen testing in the blood supply from 1972; some regional centres were using the test earlier.
(3) At the same time, in view of outbreaks of hepatitis in renal dialysis units, central advice was issued on hygiene precautions (based on local practices), and the use of testing

in renal units; testing was coordinated by the central PHLS.
(4) In 1975, hepatitis B was scheduled as an industrial injury for workers in 'close and frequent' contact with sources of possible infection, whether infected patients or blood.
(5) In 1979, advice was given to dentists on which patients to regard as hepatitis risks, how to treat them, and which to refer to special dental units.
(6) In 1981, the DHSS issued guidelines for health authorities on hepatitis B and NHS staff, reinforcing confidentiality and the worker's right not to be tested unless, following attacks of jaundice among patients, they were identified as a probable source of infection.
(7) In 1982, guidelines on hepatitis B vaccination targetted health workers covered by 1975 legislation, and groups mentioned in the 1979 dentists' guidelines.
(8) In 1988, vaccine guidelines were broadened to include 'lifestyle' groups (gays, IVDUs), but without resources to ensure they were reached.
(9) In 1993, guidelines on health workers and hepatitis B lifted restrictions on HBsAg carriers who were not positive for the 'e' antigen, and promoted vaccination for all workers who might face contact with the disease, including students.

Before 1968, the picture of hepatitis B was chiefly based on outbreaks of acute disease, but after the antigen test became available, a more complex picture of carrier prevalence in different populations and sub-groups was established. The disease had been first noted (but not yet defined) in the early twentieth century among people undergoing inoculations

and patients receiving arsenic therapy for venereal disease; to these were added during the Second World War: transfusion recipients; family contacts of those with the disease; and inmates of institutions for the mentally handicapped. In the postwar period many other categories were added, principally: IVDUs; doctors, nurses and other health workers in hospitals and clinical laboratories; homosexual men; haemophiliacs receiving Factor VIII; and infants of carrier mothers.

As indicated in the summary of policy inputs, research findings on risk groups did not determine policy. Nor did new technologies resulting from research - a test in the 1970s and a vaccine in the 1980s - necessarily solve public health problems presented by hepatitis B, although these innovations made possible certain policy options that were not previously on the agenda. Throughout this thesis, it has been suggested that changing constructions of hepatitis B mediated between research and policy. The perception of diseases, by doctors, by policy makers or by the wider public, is not solely a matter of scientific 'facts' (which in any case, as we have just seen in the case of hepatitis B, may change greatly over time) but depends also on social attitudes towards the activities or places associated with spread of the disease. Thus sexually contagious diseases take on moral overtones (or undertones); those spread via food or water, through faecal contamination, arouse anxieties over pollution and corruption of the wider social fabric; while diseases like typhus which spread by vectors thought to thrive in filthy conditions have, in the past, been tied in with theories of social hygiene.

Hepatitis B could have been constructed as a sexually transmitted disease, like AIDS, and indeed it has increasingly been seen that way in the light of AIDS. But through most of the period dealt with here, hepatitis B was seen as a disease which was generated by medical interventions (inoculations, blood transfusions, kidney dialysis, Factor VIII). Concern over transmission of hepatitis as a side-effect of new health technologies was never great enough to deter application of these technologies, each in their turn regarded by clinicians as valuable life-savers.

Enormous concern was generated at what we can term 'crisis points', by particularly spectacular outbreaks: during the yellow fever inoculation campaign in wartime, and during the early years of long-term renal dialysis for chronic renal failure, in the late 1960s. The first of these spurred the government and armed forces to back MRC research into hepatitis, a rare example of direct feedback from technology-associated hepatitis into research. This did not deeply affect perceptions of the disease for most of the medical profession or policy makers, for whom 'serum hepatitis' remained a mystery, seen chiefly as a serious side-effect of transfusion. But the renal unit outbreaks led to a strong construction of the disease first as a hospital infection, then as an occupational hazard of health workers. This was to remain the dominant construction through the 1970s and 1980s, at policy level. Was this due to the Department of Health's sense of responsibility for containing the hazard on NHS premises, and keeping its workers safe? Or was it due to

agitation by the workers themselves? Or was it a result of the key role played by medical professionals as policy advisers, their concerns over the health care setting, and relative insensitivity to the problem outside that setting?

A central theme, elaborated in Chapter 6, has been the development of networks of researchers - in this study, those in London, but there are equivalent networks in rival centres such as Glasgow. Unevenly distributed technical and cognitive expertise was exchanged through this network: skills, such as EM technique, special knowledge (gained through scientific or clinical apprenticeship and practice), or use of samples collected at reference centres. These sample banks served as reference points and nodes of exchange and those in control of them became the most renowned experts. Examples include the WHO reference centre at LSHTM, headed by Zuckerman; the NLBTC, headed by Cleghorn; and key figures at the central PHLS and CDSC. The experts called on to advise the Department of Health, or the public health laboratories, on scientific and public health policy in relation to hepatitis B, included not only those who had published most papers on the subject but also those recognised by their peers as experts because of their reference role.

Medical experts played an important part in the policy process, from the wartime Jaundice Committee to the current Advisory Group on Hepatitis. Only in the former case have negotiations within the committee been open to scrutiny. However, there are hints that other hepatitis committees,

including the Rosenheim and Maycock committees as well as later advisory groups, demonstrate much continuity. Common characteristics include minimal external accountability; appointment by invitation ('who knows who'); opportunities for expansion of research opportunites and clinical empires; reaction to incidents, rather than provision of coherent overall strategies; powerful elements of surveillance with minimal feedback to the community surveyed; and a tendency to concentrate on certain valued groups (soldiers during the war, health care workers later).

While these advisory groups did not make policy, their interpretations of research - and their overall constructions of hepatitis B - were clearly influential. According to one of the medical civil servants in charge of policy on hepatitis B, there was a ranking of outside influences on the DoH via various channels: some were more welcome than others.[2] Articles in medical journals and letters from doctors (very numerous at times) had less impact than input from the CDSC ('bids for ideas', judged as more or less appropriate) or from ministers (influential but rare). A major event hitting the media could push hepatitis B up the policy agenda and give rise to ministerial concern. The most desired input was from the Advisory Group on Hepatitis. Thus, selected medical professionals act as 'gatekeepers' between the central policy machinery and the wider field of researchers and clinicians.

There are echoes here of medical control over technologies,

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[2] Interview, Hilton.

where the clinicians' cognitive expertise establishes pre-eminence over the skills of technicians.[3] Among the varying types of hepatitis researchers surveyed, (technicians, non-clinically trained scientists, and clinician researchers with technical skills), it seemed that experts were set apart from the rest by their reference role. It would be interesting to see how far the analysis offered here applies to other policy areas. A research background was often important in selection of advisers to the DoH, but the reference role might not apply, for instance, in drugs policy, where patronage of 'big chiefs' could be most crucial (the 'Maudsley mafia'). There is also evidence of genealogies of research in which hepatitis B was placed between other diseases. Several researchers came from a background of work on influenza or polio, and some talked of being 'recycled' into AIDS - and back again into hepatitis B and hepatitis C.

It seems that the practical content of policy was not necessarily generated by these central advisers. Instead, as frequently observed in this narrative, initiatives taken in local laboratories and clinical units around the country could be mediated centrally by policy advisers. For example, in the case of renal units and blood transfusion, local 'best

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[3] H. M. Marks, 'Medical technologies: social contexts and consequences', in W. Bynum and R. Porter (eds), Companion encyclopaedia of the history of medicine (New York: Routledge, 1994), Vol. 2, pp. 1592-1618; though mainly focussed on diagnostic and treatment technologies Marks' discussion makes the telling point (p. 1597) that 'physicians' assertions of clinical competence are but a sub-set of professionals' assertions of cognitive expertise', citing on such knowledge claims: A. Abbott, The system of the professions. An essay on the division of expert labour (Chicago, Illinois: University of Chicago Press, 1988)

practices' were redistributed from centre to peripheries in the form of guidelines. Some issues appear to have been under greater central control. The direction of advice on screening and vaccination tended to be one-way, from centre to peripheries. Restricted screening policies, adopted towards health care workers in the 1970s, helped to shape a restricted vaccine policy in the 1980s. There was, however, a local component in both cases, in the sense that hospitals which had suffered outbreaks of surgery-associated hepatitis B pressed for changes to central guidelines on screening; while calls by groups of nurses, or some GPs, to expand vaccine availability, may have helped influence an eventual shift in policy on vaccination (along with many other pressures).

Costs of screening and vaccination were always part of the reason for DHSS/DoH reluctance to appply these technologies to all health workers, let alone the population at large. Changes in policy, already visible (in 1993-1994) in the case of health workers, were probably precipitated by changes in the law, such as removal of crown immunity, and extension of employer liability. Whenever seriously embarrassing incidents emerged, however, the DoH was able to hide behind a double screen. On the one hand, responsibility for implementing its policies was delegated to regional or local authorities, which bore the blame, for example if a nurse bitten by a patient contracted hepatitis B. On the other hand, if central policies were challenged, the central authorities could argue that their decisions were based on the best expert advice available at the time. This happened very recently over

hepatitis C testing of blood, introduced later in the UK than in other countries in Europe, leading to an unknown number of patients being given the virus.[4]

It may be because such contentious issues are very much alive that many hepatitis experts were reluctant to be interviewed, and a cloak of secrecy shrouded the formulation of large areas of recent policy. It may also, of course, have been partly due to intense rivalries and tensions between various parties, which informants hinted at but refused to explicate.

One longstanding tendency can be seen, in issues as diverse as MacCallum's wartime experiments and screening policies in the 1970s, which it may be helpful to think of in terms of 'the importance of not knowing'.[5] In the former case, as in some recent instances, it was important that the public should not know: in the case of screening, doctors themselves preferred not to know about their hepatitis B status (in general). This made tolerable their own 'not knowing' which patients were carriers. Perhaps this notion could be extended into the recent period of vaccination policy, when official policy has included gay men and IVDUs among target groups, but studies show that the agencies that might reach out to these groups have often failed to do so, leaving clients in a state of 'not knowing' and therefore not demanding the expensive vaccine.

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[4] BBC Panorama programme, 'Bad blood', 16 Jan 1995. The programme was very partisan, benefitting from 20-20 hindsight.

[5] This phrase is adapted from anthropologist Murray Last, writing about health attitudes of non-Muslim Hausa; see: M. Last, 'The importance of knowing about not knowing', Social Science and Medicine, 15B (1981), 387-92.

It is not clear how important was 'not knowing' in the context of information passing from the medical press to the public media. Muraskin's view that health workers kept back information on hepatitis B, because they were themselves a risk group and wished to avoid the consequences of public exposure and debate, seems too conspiratorial; health workers, particularly the small but high risk category of laboratory technicians, actively raised the profile of hepatitis B in their professional journals. A more probable explanation seems to be that hepatitis B was no more exciting to the national press than most other diseases, and only received coverage when there was a crisis, such as the renal unit outbreaks. This fits with what has here been described as the 'normalizing' tendency of Rosenheim: the renal unit outbreaks may have left a scar on the collective medical psyche, but methods of coping were rapidly evolved, in line with containment of previous hospital infections.

Comparison with AIDS[6]

Perhaps the most striking dissimilarity between the histories of hepatitis B and AIDS has been the low public profile of one, and the huge public profile of the other, despite their remarkably similar patterns of transmission. Why should we expect them to have been similarly high-profile and subject to open debate, as Muraskin suggests?[7] It would have been

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[6] This will involve an impressionistic view of AIDS; I am grateful to Dr Virginia Berridge for drawing my attention to many of these parallels and contrasts.

[7] Muraskin, 'Silent epidemic'.

convenient, perhaps even commendable, if hepatitis B had paved the way for AIDS through public debate on public health versus individual rights questions over testing, screening, and care of patients; but it did not. As indicated above, the fact that health care workers were a risk group for hepatitis B but not for AIDS (a distinction now open to question) was only part of the explanation, though it is the point on which Muraskin concentrates.

Another, less conspiratorial, explanation for different media responses arises from the nature of the diseases, plus the novelty of AIDS. While the epidemiology of hepatitis B and AIDS is similar, giving cause to make comparisons, their natural histories have appeared rather dissimilar. In an apparently haphazard way, hepatitis B provoked a variety of responses, from fatal, fulminating acute hepatitis, to inapparent infection resulting decades later in liver cancer - but in most cases, no lasting damage occurred, and the fatality rate was low. AIDS, by contrast, initially appeared as a new, fatal disease, with rapidly increasing numbers of victims. The knowledge that hepatitis B, in the 1990s, kills greater numbers of people around the world than does AIDS - a claim made almost with pride, it seems, by hepatitis experts - has not shifted general perceptions of the relative threat of the diseases. For a country like the UK, AIDS is the bigger killer, though still not a very big one; and it has received immense policy attention. Hepatitis B is seen as a nasty disease, but rather on a par with many other communicable diseases, which rarely enter the public consciousness in a

sustained manner.

Muraskin may be right that public debates that could have taken place over hepatitis B did not occur, and therefore AIDS debates had to begin with a tabula rasa, but this conclusion applies only to the public arena, and not for the reason he gave. On the other hand, in the history of hepatitis B presented here, there was plenty of less public debate, among health care workers and policy advisers. Since some of these policy advisers were (in their own words) 'recycled' into AIDS, it is unsurprising to find that similar approaches emerged in the policy history of AIDS. But it should be remembered that the group of experts drawn into the policy community for AIDS was more wide-ranging than that for hepatitis B: it included leading figures in genito-urinary medicine, a previously marginalized specialty, as well as immunologists who had not worked on hepatitis B.

The predominant pattern in both cases was that the DoH turned primarily to medical professionals to interpret the disease, while other groups were given less voice in helping to form policy. For hepatitis B, one or two civil servants settled policy in consultation with advisers. For AIDS, politicians became more involved in policy debates, and there seems to have been a greater degree of intervention by bureaucrats. While it seems fair to say that the values of the biomedical elite were influential in both cases, the AIDS policy debate probably reflected broader political forces. In both cases, central advisory groups used examples of local practices in

drawing up their policy recommendations. Local responsibility for implementing policy was also important in both cases, but money was made available for AIDS work in a way that was unthinkable for hepatitis B (or for other diseases that affect much larger numbers of people).

Gay men were belatedly acknowledged as a risk group for hepatitis B, whereas they were the major focus of attention in the early days of the AIDS epidemic. Mothers and infants, already a heavily medicalized category, were subject to policy for both diseases: vaccination, for hepatitis B; screening, for AIDS. Haemophiliacs, medicalized in a different way, became victims of inadvertent transmission firstly of hepatitis, and then AIDS, through policies which some, in retrospect, saw as negligent. The biggest 'risk group' for both diseases, IVDUs, were marginalized in policies for these diseases, as they are in society as a whole. Health care workers, by contrast, were at the centre of the policy agenda, both for hepatitis B where they formed an acknowledged risk group, but also for AIDS where their position as a risk group was denied.

One potential application of a test is for screening, either populations or risk groups. There has been more open controversy over this policy issue for AIDS, but it was also a matter for debate in the case of hepatitis B. Screening for epidemiological purposes was part of hepatitis B research from the beginning, but screening of risk groups to find carriers, with an aim of acting on the findings, was scarcely ever

implemented. Health care workers were the major group under consideration for this sort of screening, for hepatitis B, but they were spared from screening, by and large. In the more urgent and open debate over screening health workers for AIDS, health care workers' objections carried weight, maybe partly due to this precedent as well as the sympathies of policy advisers who were drawn from the medical profession.

Arguments over the use of tests in the blood service, for both hepatitis and for AIDS, focussed on the issue of false positives. The danger that large numbers of blood donors would be identified as carriers, when in fact they were not, raised questions of psychological harm to the individual and harm to the blood transfusion service if many donors were lost. In the event, a hepatitis B test was introduced for whole blood very rapidly, possibly more rapidly than would have been the case had not the renal unit outbreaks created such a sense of urgency around 1970, when the test first became available. Blood products were also tested for hepatitis B, but as we have seen, they were not tested for HIV with the first available test in 1985. Then in 1990, a decision was taken against using the first test for hepatitis C, for whole blood transfusions, presumably on the grounds that too many false positives were likely.

History was used in the case of renal unit outbreaks of hepatitis B (though in a very vague manner) to establish continuity with past examples of successful containment: it might seem that this is a contrast with the use of history in

the early days of AIDS, where comparison was rather with plagues and panics of the past. But in terms of the way that policy formulation actually worked, a normalizing, 'middle of the road' strand was dominant in both cases, demonstrating continuity with past models in the Department of Health. Cost-cutting, caution and containment - the normative values of any Whitehall department - were wedded with medical and scientific values to shape policy on hepatitis B and AIDS.

Topics for future research

Themes raised by this study could be expanded in a number of ways. A central argument, about the way that 'experts' were created in the course of research, and then selected as advisers for central policy making, would merit comparison across different policy areas: other diseases, or areas such as policy on addictions. The way that a central-local dynamic has worked in policy formation could also be studied in other instances. The history of negotiations between health workers and employers, issues of health and safety, and control in laboratories and clinical settings, has been little studied for the postwar period. The way preventive measures were put in place, to some extent in return for freedom from screening, may or may not be reflected in other histories. The pattern of vaccination policy apparently shaped by these policies on preventive measures and screening, identified for hepatitis B, could be investigated especially for AIDS.

On hepatitis B itself, comparative work looking at its history

in other European countries would be rewarding: for the US, we already have Muraskin's studies. In the UK, issues raised by hepatitis B in prisons and mental institutions - why it was widespread, and why it was either denied or ignored - merit further research. The liver studies strand merits extensive amplification, with a study of genealogies and hierarchies of research. The internal dynamics of research in pharmaceutical companies, their links with academic and health service research, and efforts to promote company products, could be elaborated against a background of changing policies on the role of the market in the NHS. There is contemporary history in the making, in the battle between researchers to be first with a test (recently introduced) and then a vaccine for hepatitis C. Perhaps the greatest challenge would be to write a history of hepatitis B in developing countries, where the disease has been a major cause of adult mortality.

Concluding remarks

This study, in tracing hepatitis B research and policy in the UK from the 1940s to the present, has found that medical research rarely played a direct role in shaping health policy. As with many other diseases, constructions of hepatitis B changed over time: scientific 'facts' about the disease were not fixed, but were open to varying interpretations. Policy makers responded most rapidly to crises, more slowly to ongoing pressures. Factors other than research findings influenced policy: for example, cost was an inhibiting factor for screening, for safety precautions, possibly for testing,

and certainly for vaccination. But civil servants sought advice from medical experts in deciding most aspects of policy.

Investigation of networks of researchers helped to explain the way that certain researchers came to eminence as 'experts'. A small circle of mainly research-based experts predominated over a long period, as policy advisers to the Department of Health. Both the professional position of such advisers, and the Department's role as employer, help to explain the policy focus on health workers. However, an historically important impetus for the construction of hepatitis B as an occupational hazard for health workers, a construction which strongly shaped policy in the 1970s and 1980s, arose from outbreaks of hepatitis in renal dialysis units in the late 1960s. Removal of hepatitis B from the blood supply was possibly precipitated by this crisis, at a time when the first test for the disease was just available. Once a solution had been found to the major problem of hepatitis B in blood transfusion, policy on other public health hazards associated with hepatitis B was a matter of protracted negotiations. Divisions among health care workers, central-local interaction, and policies on AIDS in the past decade, have all played a part in determining policy outcomes. Constructions of hepatitis B, linking policy with research, have gradually changed according to these social, economic and political dynamics.

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Interviews
Documents
Reports and guidelines
Printed sources

Printed sources are frequently primary sources for history of this recent period; a division between primary and secondary sources was not deemed suitable for this listing. (For further discussion see section on 'Sources' in Introduction)
Theses, seminar papers and press reports have been included under 'Printed sources'.

INTERVIEWS

I would like to thank again all the informants who spared time to talk to me about hepatitis B, and to emphasize that this in no way represents an exhaustive list of possible informants. Locations of interviews generally tally with workplace for informants currently working. See list of abbreviations, p.6. Those interviews that were taped are marked (T).

Dr June Almeida, electron microscopist, Bexhill-on-Sea, 29 Jan 1993 (T)

Anonoymous informant in contact with many hepatitis B researchers, 12 July 1991

Dr John Barbara, blood transfusion centre virologist, NLBTC, Colindale, 13 July 1992

Dr George Bath, public health physician, Northern General Hospital, Edinburgh, 20 Aug 1991 (T)

Dr John Beale, public health laboratory and pharmaceutical company virologist, Royal Society of Medicine, London, 26 Feb 1993 (T)

Sheila Brewer, nursing labour relations officer, RCN, London, 14 Dec 1992

Baruch Blumberg, virologist/geneticist, Master of Balliol College Oxford, 22 Nov 1990, 12 March 1991, 5 March 1992 (T), 25 March 1992 (T)

Brian Combridge, technician, BPL Elstree, 19 June 1991 (T)

Dr David Dane, virologist, Royal Society of Medicine, London, 6 Aug 1992, 9 Dec 1993

Dr Michael Farrell, drug policy adviser, DoH, 5 Oct 1992 (T)

Brian Gee, laboratory scientific officer & safety representative, Coventry and Warwickshire Hospital, 21 June 1991 (T)

Dr Richard Gilson, genito-urinary medicine specialist, Middlesex Hospital Medical School/James Pringle House, London, 25 Feb 1991

Group B, voluntary group of hepatitis B carriers, London, 12 May 1991

Dr Andy Hall, epidemiologist, LSHTM London, 21 Nov 1990

Dr Graham Hart, medical sociologist, Middlesex Hospital Medical School/James Pringle House, London, 6 Feb 1991

Dr Julia Heptonstall, epidemiologist, CDSC, Central PHLS, Colindale, 17 April 1991

Dr Judith Hilton, medical civil servant dealing with communicable diseases, DoH, 30 Sept 1992

Prof Colin Howard, virologist, Royal Veterinary College, 25 Nov 1992 (T)

Dr J. B. Kurtz, public health laboratory virologist, John Radcliffe Hospital Oxford, 20 Feb 1992

Dr Fred MacCallum, virologist, Goring-on-Thames, 29 April 1992

Charles Medawar, freelance researcher on medical issues, London, 28 June 1991

Dr Sheila Polakoff, epidemiologist, Royal Society of Medicine, London, 14 Oct 1992

Dr Christopher Tibbs, liver specialist, Institute of Liver Studies, King's College Hospital Medical School, London, 11 Nov 1992

Dr Elise Vandervelde, virologist, Virus Reference Laboratory, Central PHLS Colindale, 1 April 1992

Prof Roger Williams, Director of Institute of Liver Studies, King's College Hospital Medical School, London, 14 Dec 1992 (T)

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MRC 3217/8, Jaundice - Transmission to volunteers

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D. S. Dane, corr. with author, 15 letters, & enclosures.

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